526 Rec'd PCT/PTO 04 DEC 2000

09/701824

Practitioner's Docket No. 776-009999-US(PAR)

CHAPTER II

Preliminary Classification:

Proposed Class:

Subclass:

NOTE: *"All applicants are requested to include a preliminary classification on newly filed patent applications. The preliminary classification, preferably class and subclass designations, should be identified in the upper right-hand corner of the letter of transmittal accompanying the application papers, for example 'Proposed Class 2, subclass 129.'" M.P.E.P., § 601, 7th ed.*

TRANSMITTAL LETTER TO THE UNITED STATES ELECTED OFFICE (EO/US)

(ENTRY INTO U.S. NATIONAL PHASE UNDER CHAPTER II)

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/CA99/00529	4 June 1999	4 June 1998

TITLE OF INVENTION

Proportional Pressure Assist Ventilation Controlled By A Diaphragm Electromyographic Signal

APPLICANT(S)

Christer SINDERBY, Jennifer BECK

Box PCT
Assistant Commissioner for Patents
Washington D.C. 20231

ATTENTION: EO/US

CERTIFICATION UNDER 37 C.F.R. § 1.10*
(Express Mail label number is mandatory.)
(Express Mail certification is optional.)

I hereby certify that this Transmittal Letter and the papers indicated as being transmitted therewith is being deposited with the United States Postal Service on this date 4 December 2000, in an envelope as "Express Mail Post Office to Addressee" Mailing Label Number EL627419991OUS, addressed to the: Assistant Commissioner for Patents, Washington, D.C. 20231.

Deborah J. Clark

(type or print name of person mailing paper)

Deborah J. Clark

Signature of person mailing paper

WARNING: *Certificate of mailing (first class) or facsimile transmission procedures of 37 C.F.R. § 1.8 cannot be used to obtain a date of mailing or transmission for this correspondence.*

"WARNING: *Each paper or fee filed by "Express Mail" **must** have the number of the "Express Mail" mailing label placed thereon prior to mailing. 37 C.F.R. § 1.10(b).*
*"Since the filing of correspondence under § 1.10 without the Express Mail mailing label thereon is an oversight that can be avoided by the exercise of reasonable care, requests for waiver of this requirement will **not** be granted on petition." Notice of Oct. 24, 1996, 60 Fed. Reg. 56,439, at 56,442.*

NOTE: To avoid abandonment of the application, the applicant shall furnish to the USPTO, not later than 20 months from the priority date: (1) a copy of the international application, unless it has been previously communicated by the International Bureau or unless it was originally filed in the USPTO; and (2) the basic national fee (see 37 C.F.R. § 1.492(a)). The 30-month time limit may not be extended. 37 C.F.R. § 1.495.

***WARNING:** Where the items are those which can be submitted to complete the entry of the international application into the national phase are subsequent to 30 months from the priority date the application is still considered to be in the international state and if mailing procedures are utilized to obtain a date the express mail procedure of 37 C.F.R. § 1.10 must be used (since international application papers are not covered by an ordinary certificate of mailing—See 37 C.F.R. § 1.8.*

NOTE: Documents and fees must be clearly identified as a submission to enter the national state under 35 U.S.C. § 371 otherwise the submission will be considered as being made under 35 U.S.C. § 111. 37 C.F.R. § 1.494(f).

I. Applicant herewith submits to the United States Elected Office (EO/US) the following items under 35 U.S.C. § 371:

a. ☒ This express request to immediately begin national examination procedures (35 U.S.C. § 371(f)).

b. ☒ The U.S. National Fee (35 U.S.C. § 371(c)(1)) and other fees (37 C.F.R. § 1.492) as indicated below:

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2. Fees

CLAIMS FEE	(1) FOR	(2) NUMBER FILED	(3) NUMBER EXTRA	(4) RATE	(5) CALCULATIONS
☐*	TOTAL CLAIMS 59	59 −20=	39	× $18.00=	$ 702.00
	INDEPENDENT CLAIMS 6	6 −3=	3	×$80.00	240.00
	MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ $270.00	
BASIC FEE**	☐ U.S. PTO WAS INTERNATIONAL PRELIMINARY EXAMINATION AUTHORITY Where an International preliminary examination fee as set forth in § 1.482 has been paid on the international application to the U.S. PTO: ☐ and the international preliminary examination report states that the criteria of novelty, inventive step (non-obviousness) and industrial activity, as defined in PCT Article 33(1) to (4) have been satisfied for all the claims presented in the application entering the national stage (37 C.F.R. § 1.492(a)(4)) ..... $100.00 ☐ and the above requirements are not met (37 C.F.R. § 1.492(a)(1)) ..... $690.00 ☒ U.S. PTO WAS NOT INTERNATIONAL PRELIMINARY EXAMINATION AUTHORITY Where no international preliminary examination fee as set forth in § 1.482 has been paid to the U.S. PTO, and payment of an international search fee as set forth in § 1.445(a)(2) to the U.S. PTO: ☐ has been paid (37 C.F.R. § 1.492(a)(2)) ..... $710.00 ☐ has not been paid (37 C.F.R. § 1.492(a)(3)) ..... $1,000. ☒ where a search report on the international application has been prepared by the European Patent Office or the Japanese Patent Office (37 C.F.R. § 1.492(a)(5)) $860.00				860.00
	Total of above Calculations				= 1,802.00
SMALL ENTITY	Reduction by 1/2 for filing by small entity, if applicable. Affidavit must be filed also. (note 37 C.F.R. § 1.9, 1.27, 1.28)				901.00
	Subtotal				$901.00
	Total National Fee				$ 901.00
	Fee for recording the enclosed assignment document $40.00 (37 C.F.R. § 1.21(h)). (See Item 13 below). See attached "ASSIGNMENT COVER SHEET".				
TOTAL	Total Fees enclosed				$ 901.00

*See attached Preliminary Amendment Reducing the Number of Claims.

i. ☒ A check in the amount of $901.00 to cover the above fees is enclosed.

ii. ☐ Please charge Account No. _____ in the amount of $ _____. A duplicate copy of this sheet is enclosed.

***WARNING:** *"To avoid abandonment of the application the applicant shall furnish to the United States Patent and Trademark Office not later than the expiration of 30 months from the priority date: * * * (2) the basic national fee (see § 1.492(a)). The 30-month time limit may not be extended." 37 C.F.R. § 1.495(b).*

WARNING: *If the translation of the international application and/or the oath or declaration have not been submitted by the applicant within thirty (30) months from the priority date, such requirements may be met within a time period set by the Office. 37 C.F.R. § 1.495(b)(2). The payment of the surcharge set forth in § 1.492(e) is required as a condition for accepting the oath or declaration later than thirty (30) months after the priority date. The payment of the processing fee set forth in § 1.492(f) is required for acceptance of an English translation later than thirty (30) months after the priority date. Failure to comply with these requirements will result in abandonment of the application. The provisions of § 1.136 apply to the period which is set. Notice of Jan. 3, 1993, 1147 O.G. 29 to 40.*

3. ☒ A copy of the International application as filed (35 U.S.C. § 371(c)(2)):

NOTE: Section 1.495 (b) was amended to require that the basic national fee and a copy of the international application must be filed with the Office by 30 months from the priority date to avoid abandonment. "The International Bureau normally provides the copy of the international application to the Office in accordance with PCT Article 20. At the same time, the International Bureau notifies applicant of the communication to the Office. In accordance with PCT Rule 47.1, that notice shall be accepted by all designated offices as conclusive evidence that the communication has duly taken place. Thus, if the applicant desires to enter the national stage, the applicant normally need only check to be sure the notice from the International Bureau has been received and then pay the basic national fee by 30 months from the priority date." Notice of Jan. 7, 1993, 1147 O.G. 29 to 40, at 35-36. See item 14c below.

a. ☒ is transmitted herewith.

b. ☐ is not required, as the application was filed with the United States Receiving Office.

c. ☐ has been transmitted

i. ☐ by the International Bureau.
Date of mailing of the application (from form PCT/1B/308): _____.

ii. ☐ by applicant on _____.
Date

4. ☒ A translation of the International application into the English language (35 U.S.C. § 371(c)(2)):

a. ☐ is transmitted herewith.

b. ☒ is not required as the application was filed in English.

c. ☐ was previously transmitted by applicant on _____.
Date

d. ☐ will follow.

5. [X] Amendments to the claims of the International application under PCT Article 19 (35 U.S.C. § 371(c)(3)):

NOTE: *The Notice of January 7, 1993 points out that 37 C.F.R. § 1.495(a) was amended to clarify the existing and continuing practice that PCT Article 19 amendments must be submitted by 30 months from the priority date and this deadline may not be extended. The Notice further advises that: "The failure to do so will not result in loss of the subject matter of the PCT Article 19 amendments. Applicant may submit that subject matter in a preliminary amendment filed under section 1.121. In many cases, filing an amendment under section 1.121 is preferable since grammatical or idiomatic errors may be corrected." 1147 O.G. 29-40, at 36.*

a. [ ] are transmitted herewith.

b. [ ] have been transmitted

i. [ ] by the International Bureau.
Date of mailing of the amendment (from form PCT/1B/308): _____.

ii. [ ] by applicant on (date) _____.
Date

c. [X] have not been transmitted as

i. [X] applicant chose not to make amendments under PCT Article 19.
Date of mailing of Search Report (from form PCT/ISA/210.): 6/10/99

ii. [ ] the time limit for the submission of amendments has not yet expired. The amendments or a statement that amendments have not been made will be transmitted before the expiration of the time limit under PCT Rule 46.1.

6. [ ] A translation of the amendments to the claims under PCT Article 19 (38 U.S.C. § 371(c)(3)):

a. [ ] is transmitted herewith.

b. [ ] is not required as the amendments were made in the English language.

c. [ ] has not been transmitted for reasons indicated at point 5(c) above.

7. [X] A copy of the international examination report (PCT/IPEA/409)

[XX] is transmitted herewith.

[ ] is not required as the application was filed with the United States Receiving Office.

8. [X] Annex(es) to the international preliminary examination report

a. [X] is/are transmitted herewith.

b. [ ] is/are not required as the application was filed with the United States Receiving Office.

9. [X] A translation of the annexes to the international preliminary examination report

a. [ ] is transmitted herewith.

b. [X] is not required as the annexes are in the English language.

10. ☒ An oath or declaration of the inventor (35 U.S.C. § 371(c)(4)) complying with 35 U.S.C. § 115

a. ☐ was previously submitted by applicant on _____. Date

b. ☐ is submitted herewith, and such oath or declaration

i. ☐ is attached to the application.

ii. ☐ identifies the application and any amendments under PCT Article 19 that were transmitted as stated in points 3(b) or 3(c) and 5(b); and states that they were reviewed by the inventor as required by 37 C.F.R. § 1.70.

iii. ☒ will follow.

II. Other document(s) or information included:

11. ☒ An International Search Report (PCT/ISA/210) or Declaration under PCT Article 17(2)(a):

a. ☒ is transmitted herewith.

b. ☐ has been transmitted by the International Bureau. Date of mailing (from form PCT/IB/308): _____.

c. ☐ is not required, as the application was searched by the United States International Searching Authority.

d. ☐ will be transmitted promptly upon request.

e. ☐ has been submitted by applicant on _____. Date

12. ☒ An Information Disclosure Statement under 37 C.F.R. §§ 1.97 and 1.98:

a. ☐ is transmitted herewith.

Also transmitted herewith is/are:

☐ Form PTO-1449 (PTO/SB/08A and 08B).

☐ Copies of citations listed.

b. ☒ will be transmitted within THREE MONTHS of the date of submission of requirements under 35 U.S.C. § 371(c).

c. ☐ was previously submitted by applicant on _____. Date

13. ☐ An assignment document is transmitted herewith for recording.

A separate ☐ "COVER SHEET FOR ASSIGNMENT (DOCUMENT) ACCOMPANYING NEW PATENT APPLICATION" or ☐ FORM PTO 1595 is also attached.

_____ _____

_____ _____

_____ _____

14. [X] Additional documents:
    a. [XX] Copy of request (PCT/RO/101)
    b. [XX] International Publication No. WO 99/62580
        i. [ ] Specification, claims and drawing
        ii. [XX] Front page only
    c. [XX] Preliminary amendment (37 C.F.R. § 1.121)
    d. [XX] Other
    Amendments under Article 34, Demand, Written Opinion, Response to Written Opinion , Preliminary Examination Report

15. [X] The above checked items are being transmitted
    a. [X] before 30 months from any claimed priority date.
    b. [ ] after 30 months.

16. [ ] Certain requirements under 35 U.S.C. § 371 were previously submitted by the applicant on _____, namely:

AUTHORIZATION TO CHARGE ADDITIONAL FEES

WARNING: *Accurately count claims, especially multiple dependant claims, to avoid unexpected high charges if extra claims are authorized.*

NOTE: "A written request may be submitted in an application that is an authorization to treat any concurrent or future reply, requiring a petition for an extension of time under this paragraph for its timely submission, as incorporating a petition for extension of time for the appropriate length of time. An authorization to charge all required fees, fees under § 1.17, or all required extension of time fees will be treated as a constructive petition for an extension of time in any concurrent or future reply requiring a petition for an extension of time under this paragraph for its timely submission. Submission of the fee set forth in § 1.17(a) will also be treated as a constructive petition for an extension of time in any concurrent reply requiring a petition for an extension of time under this paragraph for its timely submission." 37 C.F.R. § 1.136(a)(3).

NOTE: "Amounts of twenty-five dollars or less will not be returned unless specifically requested within a reasonable time, nor will the payer be notified of such amounts; amounts over twenty-five dollars may be returned by check or, if requested, by credit to a deposit account." 37 C.F.R. § 1.26(a).

[X] The Commissioner is hereby authorized to charge the following additional fees that may be required by this paper and during the entire pendency of this application to Account No. 16-1350.

[X] 37 C.F.R. § 1.492(a)(1), (2), (3), and (4) (filing fees)

WARNING: *Because failure to pay the national fee within 30 months without extension (37 C.F.R. § 1.495(b)(2)) results in abandonment of the application, it would be best to always check the above box.*

☒ 37 C.F.R. § 1.492(b), (c) and (d) (presentation of extra claims)

NOTE: Because additional fees for excess or multiple dependent claims not paid on filing or on later presentation must only be paid or these claims cancelled by amendment prior to the expiration of the time period set for response by the PTO in any notice of fee deficiency (37 C.F.R. § 1.492(d)), it might be best not to authorize the PTO to charge additional claim fees, except possible when dealing with amendments after final action.

☒ 37 C.F.R. § 1.17 (application processing fees)

☐ 37 C.F.R. § 1.17(a)(1)–(5) (extension fees pursuant to § 1.136(a).

☐ 37 C.F.R. § 1.18 (issue fee at or before mailing of Notice of Allowance, pursuant to 37 C.F.R. § 1.311(b))

NOTE: Where an authorization to charge the issue fee to a deposit account has been filed before the mailing of a Notice of Allowance, the issue fee will be automatically charged to the deposit account at the time of mailing the notice of allowance. 37 C.F.R. § 1.311(b).

NOTE: 37 C.F.R. § 1.28(b) requires "Notification of any change in loss of entitlement to small entity status must be filed in the application . . . prior to paying, or at the time of paying . . . issue fee." From the wording of 37 C.F.R. § 1.28(b): (a) notification of change of status must be made even if the fee is paid as "other than a small entity" and (b) no notification is required if the change is to another small entity.

☒ 37 C.F.R. § 1.492(e) and (f) (surcharge fees for filing the declaration and/or filing an English translation of an International Application later than 30 months after the priority date).

PLEASE SEND ALL CORRESPONDENCE TO:

Reg. No.: 24,622

Tel. No.: (203) 259-1800

Customer No.: 2512

SIGNATURE OF PRACTITIONER

Clarence A. Green

(type or print name of practitioner)

PERMAN & GREEN, LLP

P.O. Address

425 Post Road, Fairfield, Connecticut 06430, USA

PLEASE SEND ALL CORRESPONDENCE TO:

Clarence A. Green
PERMAN & GREEN, LLP
425 Post Road, Fairfield, Connecticut 06430, USA

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Express Mail No.: EL627419910US

In re Application of: SINDERBY et al.

INTERNATIONAL APPLICATION NO.: PCT/CA99/00529

INTERNATIONAL FILING DATE: 4 June 1999

U.S. SERIAL NUMBER:

FILING DATE: Herewith

TITLE: PROPORTIONAL PRESSURE ASSIST VENTILATION CONTROLLED BY A DIAPHRAGM ELECTROMYOGRAPHIC SIGNAL

ATTORNEY DOCKET NO.: 776-009999-US(PAR)

Box PCT
The Commissioner of Patents and Trademarks
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Dear Sir:

Please amend the above-identified, enclosed patent application as follows:

IN THE SPECIFICATION

On page 1 of the specification, please delete the title "Automatic Adjustment Of Applied Levels Of Ventilatory Support And Extrinsic Peep By Closed-Loop Control of Neuro-Ventilatory Efficiency" and insert the new title as follows:

--PROPORTIONAL PRESSURE ASSIST VENTILATION CONTROLLED BY A DIAPHRAGM ELECTROMYOGRAPHIC SIGNAL--

IN THE CLAIMS:

Please amend Claims 3, 4, 5, 6, 9, 10, 11, 12, 16, 17, 18, 19, 20, 21, 22, 23, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 39, 40, 41, 42, 44, 45, 46, 47, 51, 52, 53, 54, 56, 57, 58 and 59 as shown below.

Claim 3, line 2, delete "or 2".

Claim 4, line 2, delete "2 or 3,".

Claim 5, line 2, delete "2, 3 or 4,".

Claim 6, line 2, delete "2, 3, 4 or 5,".

Claim 9, line 2, delete "or 8".

Claim 10, line 2, delete "or 8".

Claim 11, line 2, delete "8 or 9,".

Claim 12, line 2, delete "8, 9, 10 or 11,".

Claim 16, line 2, delete "14 or 15,".

Claim 17, line 2, delete "14, 15 or 16,".

Claim 18, line 2, delete "14, 15, 16 or 17,".

Claim 19, line 2, delete "14, 15, 16, 17 or 18,".

Claim 20, line 2, delete "14, 15, 16, 17, 18 or 19,".

Claim 21, line 2, delete “14, 15, 16, 17, 18, 19 or 20,”.

Claim 22, line 2, delete “14, 15, 16, 17, 18, 19 or 20,”.

Claim 23, line 2, delete “14, 15, 16, 17, 18, 19, 20, 21 or 22”.

Claim 26, lines 1 and 2, delete “or 25”.

Claim 27, line 2, delete “or 25,”.

Claim 28, lines 1 and 2, delete “any one of claims 25 to 27” and insert --claim 25--.

Claim 29, lines 1 and 2, delete “any one of claims 24 to 28” and insert --claim 24--.

Claim 30, lines 1 and 2, delete “any one of claims 24 to 28” and insert --claim 24--.

Claim 31, lines 1 and 2, delete “any one of claims 24 to 30” and insert --claim 24--.

Claim 32, lines 1 and 2, delete “any one of claims 24 to 31” and insert --claim 24--.

Claim 33, lines 1 and 2, delete “any one of claims 22 to 32” and insert --claim 22--.

Claim 34, lines 1 and 2, delete “any one of claims 24 to 32” and insert --claim 24--.

Claim 35, lines 1 and 2, delete “any one of claims 24 to 34” and insert --claim 24--.

Claim 39, line 2, delete “any one of claims 36 to 38” and insert --claim 36--.

Claim 40, line 2, delete “any one of claims 36 to 39” and insert --claim 36--.

Claim 41, line 2, delete “any one of claims 36 to 39” and insert --claim 36--.

Claim 42, line 2, delete “any one of claims 36 to 39” and insert --claim 36--.

Claim 44, line 2, delete “any one of claims 36 to 43” and insert --claim 36--.

Claim 45, line 2, delete “any one of claims 36 to 44” and insert --claim 36--.

Claim 46, line 2, delete “any one of claims 36 to 45” and insert --claim 36--.

Claim 47, line 2, delete “any one of claims 36 to 46” and insert --claim 36--.

Claim 51, line 2, delete “any one of claims 48 to 50” and insert --claim 48--.

Claim 52, line 2, delete “any one of claims 48 to 51” and insert --claim 48--.

Claim 53, line 2, delete “any one of claims 48 to 51” and insert --claim 48--.

Claim 54, line 2, delete “any one of claims 48 to 51” and insert --claim 48--.

Claim 56, line 2, delete “any one of claims 48 to 55” and insert --claim 48--.

Claim 57, line 2, delete “any one of claims 48 to 56” and insert --claim 48--.

Claim 58, line 2, delete “any one of claims 48 to 57” and insert --claim 48--.

Claim 59, line 2, delete “any one of claims 48 to 58” and insert --claim 48--.

REMARKS

Please enter this preliminary amendment prior to calculation of the fees.

Respectfully submitted,

Clarence A. Green Reg. No.: 24,622

4 Dec 2000

Date

PERMAN & GREEN, LLP
425 Post Road, Fairfield, CT 06430
(203) 259-1800
Customer No.: 2512

AUTOMATIC ADJUSTMENT OF APPLIED LEVELS OF VENTILATORY SUPPORT AND EXTRINSIC PEEP BY CLOSED-LOOP CONTROL OF NEURO-VENTILATORY EFFICIENCY

BACKGROUND OF THE INVENTION

1. Field of the invention:

The present invention relates to a system using the intensity of the diaphragm electromyogram (EMG) at a given lung volume or the lung volume at a given EMG intensity to automatically or manually adjust the level of inspiratory support in proportion to changes in the neuro-ventilatory efficiency.

The present invention also relates to a system responsive to the intensity of the diaphragm electromyogram (EMG) measured immediately before the onset of inspiratory flow to automatically or manually control and maintain an optimum level of extrinsic positive end expiratory pressure (PEEP) applied to a patient, and to automatically or manually control a duration from the onset of EMG to onset of respiratory flow.

2. Brief description of the prior art:

Prior art algorithms used to create closed-loop ventilator systems are based on variables such as tidal volume, respiratory rate,

inspiratory flow, end-tidal carbon dioxide levels and/or rate of rise in pressure. However, none of these parameters can provide a reliable measure of the respiratory neural drive because they are affected by changes in neuro-mechanical or neuro-ventilatory efficiency.

Neuro-ventilatory efficiency is a term used to express the amount of neural drive (breathing effort) needed to obtain a given tidal lung volume. In brief, neural drive is converted into mechanical tension, a process which is influenced by the muscle length, temperature, electrolyte imbalance, etc. The role of inspiratory flow in the link between neural drive and mechanical tension has previously been suggested; however the proposed influence could not be demonstrated for mean inspiratory flow rates up to 1.4 liters/second. The mechanical tension is then translated into pressure, a process which is affected by the shape of the diaphragm dome. Finally the pressure expands the alveoli and causes air to flow, and the translation of pressure to volume depends on the elasto-viscous behaviour of the respiratory system. Consequently, there are many factors that may influence the tidal volume output obtained for a given increase in neural drive (inspiratory effort).

Evaluation of respiratory drive by measurements such as the rate of rise in pressure or lung volume is not reliable when, for example, the muscle length or the respiratory system impedance are affected by changes in the neuro-ventilatory efficiency. In a patient, airway resistance and elastance can change from one minute to another and muscle length is continuously altered.

OBJECTS AND SUMMARY OF THE INVENTION

An object of the present invention is therefore to eliminate the drawbacks of the prior art.

Another object of the present invention is to provide a closed loop system using:

(a) the Intensity of the diaphragm electromyogram (EMG) for a given inspiratory volume;

(b) the inspiratory volume for a given EMG intensity; or

(c) a combination of (a) and (b);

in view of controlling the level of gas flow, gas volume or gas pressure delivered by a mechanical (lung) ventilator; the closed loop ventilator system enables for automatic or manual adjustment of the level of inspiratory support in proportion to changes in the neuro-ventilatory efficiency such that the neural drive remains stable at a desired target level. An alarm can also be used to detect changes in neuroventilatory efficiency in view of performing manual adjustments.

Another object of the present invention is to provide a closed-loop system responsive to the intensity of the diaphragm EMG measured immediately before the onset of inspiratory flow to quantify pre-inspiratory breathing effort in view of automatically or manually adjusting

a level of extrinsic positive end expiratory pressure (PEEP) applied to a patient in proportion to changes in EMG intensity of pre-inspiratory efforts. In this manner, the pre-ventilatory intensity of the diaphragm EMG can be maintained at a desired, minimum level such that the pre-inspiratory neural drive remains stable at a desired target minimal level. Determination of the duration from the onset of EMG to the onset of respiratory flow is also used for quantitative evaluation of the intrinsic PEEP, and to guide adjustment of the trigger sensitivity of the ventilator systems.

Different from pressure and ventilatory related indexes, the intensity of the EMG represents the temporal (mean MU (motor unit) rate coding) and spatial (MU recruitment) summation of action potentials and is obtained at the level of the sarcolemma muscle. The intensity of the EMG is therefore not affected by changes in the muscle's neuro-ventilatory coupling. In the present invention, the use of crural diaphragm EMG rests on the assumption that neural drive to the crural diaphragm is representative for the total respiratory drive. It is also based on the condition that neuromuscular transmission and innervation of the crural diaphragm are normal. For breathing with increased demand this assumption is well founded. Hence, the intensity of the EMG needed to produce a given inspiratory volume should express the efficiency relation between neural drive and volume output.

The objects, advantages and other features of the present invention will become more apparent upon reading of the following non restrictive description of a preferred embodiment thereof,

given by way of example only with reference to the accompanying drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

In the appended drawings:

Figure 1 is a schematic representation of a set-up of an EMG analysis system;

Figure 2 is a section of oesophageal catheter on which an array of electrodes of the EMG analysis system of Figure 1 is mounted;

Figure 3 illustrates a section of oesophageal catheter on which a second embodiment of the array of electrodes is mounted;

Figure 4 is a graph showing a set of EMG signals of the diaphragm (EMGdi signals) detected by pairs of successive electrodes of the array of Figure 2;

Figure 5 is a flow chart showing a method for conducting a double subtraction technique of the EMGdi signals;

Figure 6 is a graph showing the distribution of correlation coefficients calculated for determining the position of the center of the

depolarizing region of the diaphragm along the array of electrodes of Figure 2;

Figure 7 is a schematic diagram illustrating in the time domain a double subtraction technique for improving the signal-to-noise ratio and to reduce an electrode-position-induced filter effect along the array of electrodes of Figure 2;

Figure 8a is a graph showing the power density spectrum of electrode motion artifacts, the power density spectrum of ECG, and the power density spectrum of EMGdi signals;

Figure 8b is a graph showing an example of transfer function for a filter to be used for filtering out the electrode motion artifacts, ECG, and the 50 or 60 Hz disturbance from electrical mains;

Figure 9 is a schematic diagram illustrating in the frequency domain stabilization by the double subtraction technique of the center frequency upon displacement of the center of the depolarizing region of the diaphragm along the array of electrodes of Figure 2;

Figure 10 is a schematic block diagram of a system according to the invention for controlling inspiratory assist by means of an EMGdi signal obtained with the above mentioned double subtraction technique and a measurement of the volume of air breathed by the patient by a commercially available system;

Figure 11 is a schematic block diagram of a system according to the invention (a) capable to determine the time delay from the onset of EMG to the onset of inspiratory flow and (b) using the level of pre-inspiratory effort obtained through the EMGdi signal intensity (common noise level subtracted) during a predetermined time period immediately preceding the onset of inspiratory flow to indicate the presence of "intrinsic PEEP" and to adjust the level of applied "extrinsic PEEP" and/or ventilator trigger sensitivity such that the level of pre-inspiratory effort is suppressed, i.e the EMGdi signal intensity (common noise level subtracted) during the above mentioned predetermined time period is close to zero;

Figure 12a is an exemplary graph of a patient's inspiratory flow versus time for quiet breathing in COPD (Chronic Obstructive Pulmonary Disease); and

Figure 12b is an exemplary graph of a patient's EMG RMS intensity versus time for quiet breathing in COPD.

DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENT

Although the preferred embodiment of the present invention will be described in relation to a double subtracted EMGdi signal, it should be kept in mind that the concept of the present invention can be used with any respiratory muscle signal.

To measure EMG activity of the diaphragm 11 (EMGdi) of a human patient 14, an array of electrodes such as 12 (Figures 1 and 2) are mounted on the free end section 15 of an oesophageal catheter 13, with a constant inter-electrode distance d (Figure 2). As shown in Figure 1, the catheter 13 is introduced into the patient's oesophagus through one nostril or the mouth until the array of electrodes 12 is situated at the level of the gastroesophageal junction. The diaphragm 11 and/or the oesophagus slightly move during breathing of the patient 14 whereby the array of electrodes 12 also slightly moves about the diaphragm 11. As will be explained in the following description, automatic compensation for this displacement is provided for.

According to a preferred embodiment, an electrode 12 is mounted on the free end section 15 of the catheter 13 by winding stainless steel wire (not shown) around that catheter 13. The wound stainless steel wire presents a rough surface smoothed out by solder, which in turn is electroplated with nickel, copper and then gold or silver. Of course, it is within the scope of the present invention to use other electrode structures. Also, the electrodes 12 can possibly be applied to a nasogastric feeding tube (not shown) which is routinely introduced in intensive-care unit (ICU) patients.

Electric wires (not shown) interconnect each pair of successive electrodes such as 1-7 (Figure 2) with a respective one of a group of differential amplifiers 16. Obviously, these electric wires follow the catheter 13 from the respective electrodes 12 to the corresponding amplifiers 16, and are preferably integrated to the catheter 13. Preferably, the electric wires transmitting the EMGdi signals collected by

the various pairs 1-7 of electrodes 12 are shielded to reduce the influence of external noise, in particular disturbance from the 50 or 60 Hz current and voltage of the electrical mains.

The group of differential amplifiers 16 amplifies (first subtraction step of a so-called double subtraction technique) and band-pass filters each EMGdi signal. This first subtraction step may also be carried out in the personnal computer 19 when the amplifiers 16 are single-ended or equivalently designed amplifiers (monopolar readings).

In the example illustrated in Figures 1 and 2, the free end section 15 of the catheter 13 is provided with an array of eight electrodes 12 defining seven pairs 1, 2, 3, 4, 5, 6 and 7 of successive electrodes 12 respectively collecting seven different EMGdi signals. Although it has been found that EMG activity of the diaphragm (EMGdi) can be measured accurately with an oesophageal catheter 13 provided on the free end section 15 thereof with an array of eight electrodes 12, a different number and/or configuration of pairs of electrodes 12 can be contemplated depending on the patient's anatomy and movement of the diaphragm. Also, the pairs 1-7 do not need to be pairs of successive electrodes; as an example Figure 3 illustrates an array of nine electrodes to form seven overlapping pairs of electrodes 1-7.

A major problem in recording EMGdi signals is to maintain the noise level as low and as constant as possible. Since the electric wires transmitting the EMGdi signals from the electrodes 12 to the differential amplifiers 16 act as an antenna, it is crucial, as indicated in the foregoing description, to shield these electric wires to thereby protect the

EMGdi signals from additional artifactual noise. Also, the package enclosing the differential amplifiers 16 is preferably made as small as possible (miniaturized) and is positioned in close proximity to the patient to decrease as much as possible the distance between the electrodes 12 and the amplifiers 16.

The amplified EMGdi signals are sampled by a personal computer 19 through respective isolation amplifiers of a unit 18, to form signal segments of fixed duration. Unit 18 supplies electric power to the various electronic components of the differential and isolation amplifiers while ensuring adequate isolation of the patient's body from such power supply. The unit 18 also incorporates bandpass filters included in the respective EMGdi signal channels to eliminate the effects of aliasing. The successive EMGdi signal segments are then digitally processed into the personal computer 19 after analog-to-digital conversion thereof. This analog-to-digital conversion is conveniently carried out by an analog-to-digital converter implemented in the personal computer 19. The personal computer 19 includes a monitor 40 and a keyboard 31.

It is believed to be within the capacity of those of ordinary skill in the art to construct suitable differential amplifiers 16 and an adequate isolation amplifiers and power supply unit 18. Accordingly, the amplifiers 16 and the unit 18 will not be further described in the present specification.

An example of the seven EMGdi signals collected by the pairs 1-7 of successive electrodes 12 (Figures 1 and 2) and supplied to the computer 19 is illustrated in Figure 4.

As the diaphragm is generally perpendicular to the longitudinal axis of the oesophageal catheter 13 equipped with an array of electrodes 12, only a portion of the electrodes 12 are situated in the vicinity of the diaphragm. It is therefore important to determine the position of the diaphragm with respect to the oesophageal electrode array.

The portion of the crural diaphragm 11 which forms the muscular tunnel through which the oesophageal catheter 13 is passed is referred to the "diaphragm depolarizing region" (DDR). The thickness of the DDR is 20-30 mm. It can be assumed that, within the DDR, the distribution of active muscle fibers has a center from which the majority of the EMGdi signals originate, i.e. the "diaphragm depolarizing region center" (DDR center). Therefore, EMGdi signals detected on opposite sides of the DDR center will be reversed in polarity with no phase shift; in other words, EMGdi signals obtained along the electrode array are reversing in polarity at the DDR center.

Moving centrally from the boundaries of the DDR, EMGdi power spectrums progressively attenuate and enhance in frequency. Reversal of signal polarity on either side of the electrode pair 4 with the most attenuated power spectrum confirms the position from which the EMGdi signals originate, the DDR center.

Referring to Figure 5, the first task of the computer 19 is to determine the position of the center of the DDR along the array of electrodes 12. The center of the DDR is repeatedly determined at predetermined time intervals.

For that purpose, filtering step 505 removes from each EMGdi signal the motion artifacts, the electrocardiogram (ECG) component, and the disturbance from the electrical mains. Motion artifacts are induced by motion of the electrodes 12. More generally, motion artifacts are defined as a low frequency fluctuation of the EMGdi signals' DC level induced by mechanical alterations of the electrode metal to electrolyte interface i.e. changes in electrode contact area and/or changes in pressure that the tissue exerts on the electrode.

In step 501, the filtered EMGdi signals from step 505 are cross-correlated in pairs. As well known to those of ordinary skill in the art, cross-correlation is a statistical determination of the phase relationship between two signals and essentially calculates the similarity between two signals in terms of a correlation coefficient r (step 502). A negative correlation coefficient r indicates that the cross-correlated signals are of opposite polarities.

Figure 6 shows curves of the value of the correlation coefficient r versus the midpoint between the pairs of electrodes from which the correlated EMGdi signals originate. In this example, the inter-electrode distance is 10 mm. Curves are drawn for distances between the correlated pairs of electrodes 12 of 5 mm (curve 20), 10 mm (curve 21), 15 mm (curve 22) and 20 mm (curve 23). One can appreciate from Figure 5 that negative correlation coefficients r are obtained when EMGdi signals from respective electrode pairs situated on opposite sides of the electrode pair 4 are cross-correlated. It therefore appears that the change in polarity occurs in the region of electrode pair 4, which is confirmed by the curves of Figure 4. Accordingly, it can be assumed that

the center of the DDR is situated substantially midway between the electrodes 12 forming pair 4.

For example, the center of the DDR can be precisely determined by interpolation (step 503 of Figure 5) using a square law based fit of the three most negative correlation coefficients of curve 21 obtained by successive cross-correlation of the EMGdi signal segments from each electrode pair to the EMGdi signal segments from the second next electrode pair. Association of the center of the DDR to a pair of electrodes 12 provides a "reference position" from which to obtain EMGdi signal segments within the DDR. Such control is essential in overcoming the artifactual influence of perpendicular bipolar electrode filtering on the EMGdi power spectrum.

It has been experimentally demonstrated that EMGdi signals recorded in the oesophagus are satisfactory as long as they are obtained from electrode pairs (with an inter-electrode distance situated between 5 and 20 mm) positioned at a distance situated between 5 and 30 mm on the opposite sides of the DDR center (the inter-pair distance being therefore situated between 5 and 30 mm). Although EMGdi signals obtained from these positions offers a clear improvement in acceptance rate, the signal-to-noise ratio during quiet breathing still tends to remain unsatisfactorily low. The EMGdi signal obtained from one electrode pair (for example channel 0 in Figure 7) situated in between the two electrode pairs used to produce the double subtracted signal, can be added to this double subtracted signal either before as a raw signal or after when RMS or equivalent EMGdi signal measure has been computed, in order to minimize loss of signal.

For example, in Figure 4, the EMGdi signals originating from the electrode pairs 3 and 5 situated respectively 10 mm below and 10 mm above the DDR are strongly inversely correlated at zero time delay. In contrast to the inversely correlated EMGdi signals, the noise components for electrode pairs 3 and 5 are likely to be positively correlated. Hence, as illustrated in Figure 7, subtraction of the EMGdi signals 24 and 25 from electrode pairs 3 and 5 will result into an addition of the corresponding EMGdi signals (signal 26 of Figure 6) and into a subtraction, that is an elimination of the common noise components. This technique will be referred to as "the double subtraction technique" (step 504 of Figure 5). Again, the EMGdi signal obtained from one electrode pair (for example channel 0 in Figure 7) situated in between the two electrode pairs used to produce the double subtracted signal, can be added to this double subtracted signal either before as a raw signal or after when RMS or equivalent EMGdi signal measure has been computed, in order to minimize loss of signal.

Subtraction step 504 (second subtraction step of the double subtraction technique) can be carried out either in the time domain, or after conversion of signals 24 and 25 in the frequency domain. Double subtraction technique can be performed by subtracting other combinations of signals, for example by subtracting the EMGdi signal segments from electrode pair 2 from the EMGdi signal segments from electrode pair 5 (Figure 4), by subtracting signal segments from electrode pair 6 from the signal segments from electrode pair 3 and by adding these differences, etc. What is important is to subtract two signals of opposite polarities obtained in the vicinity of the muscle. More than two signal pairs of opposite polarities can be used in the double subtraction. Again,

the EMGdi signal obtained from one electrode pair (for example channel 0 in Figure 7) situated in between the two electrode pairs used to produce the double subtracted signal, can be added to this double subtracted signal either before as a raw signal or after when RMS or equivalent EMGdi signal measure has been computed, in order to minimize loss of signal.

The double subtraction technique is carried out in step 504 on the pair of EMGdi signals (for example the signals from electrode pairs 3 and 6 shown in Figure 4) identified in step 503, after appropriate filtering of these EMGdi signals in step 505. Still again, the EMGdi signal obtained from one electrode pair (for example channel 0 in Figure 7) situated in between the two electrode pairs used to produce the double subtracted signal, can be added to this double subtracted signal either before as a raw signal or after when RMS or equivalent EMGdi signal measure has been computed, in order to minimize loss of signal.

The graph of Figure 8a shows the power density spectrum of the above defined electrode motion artifacts, the power density spectrum of ECG, and the power density spectrum of EMGdi signals. The graph of Figure 8b shows an example of transfer function for a filter (the dashed line showing the optimal transfer function, and the solid line the transfer function implemented by the inventors) to be used in step 505 for filtering out the electrode motion artifacts, ECG, and the 50 or 60 Hz disturbance from the electrical mains. Processing of the EMGdi signals by the computer 19 to follow as closely as possible the optimal transfer function of Figure 8b will conduct adequately filtering step 505.

Therefore, double-subtracted signal segments 509 are obtained at the output of step 504 by subtracting the EMGdi signal segments from the pair of electrodes 12 in optimal location above the diaphragm from the EMGdi signal segments from the pair of electrodes 12 in optimal location below the diaphragm. More than two signal pairs of opposite polarities can be used in the double subtraction. Again, the EMGdi signal obtained from one electrode pair (for example channel 0 in Figure 7) situated in between the two electrode pairs used to produce the double subtracted signal, can be added to this double subtracted signal either before as a raw signal or after when RMS or equivalent EMGdi signal measure has been computed, in order to minimize loss of signal.

Referring back to Figure 5, step 506 calculates the RMS (root-mean-square) or equivalent or similar value 510 of the double-subtracted signal segments 509 produced in step 504. The increase in intensity obtained with the double subtraction technique is associated with a twofold increase in RMS values. RMS values obtained with the double subtraction technique are closely and linearly related to the original signals. It should be kept in mind that the RMS value can be replaced by any other value representative of the strength of the double-subtracted signal segments 509.

The digital RMS signal segment value 510 calculated by the computer 19 in step 506 is finally digital-to-analog converted to an on-line analog RMS value 508 (step 507) in view of controlling a lung ventilator 54 (Figure 10). It should be mentioned that it is within the scope of the present invention to supply a digital value 508.

The double subtraction technique compensates for the changes in signal strength and frequency caused by movement of the diaphragm 11 (Figure 1) and/or the oesophagus during breathing of the patient 14 causing movement of the array of electrodes 12 with respect to the diaphragm 11. Referring to Figure 9, off center of the array of electrodes 12 (electrode-position-induced filter effect) causes a variation of center frequency values due to filtering (see curves 27 and 28) for the EMGdi signals from the electrode pairs 3 and 5. The double subtraction technique eliminates such variation of center frequency values as indicated by curve 29 as well as variation of signal strength. Therefore, the reciprocal influence of the position of the DDR center on the EMGdi signal frequency content is eliminated by the double subtraction technique.

It has been found that the double subtraction technique may improve the signal-to-noise ratio by more than 2 dB and reduce an electrode-position-induced filter effect. Double subtraction technique is also responsible for a relative increase in acceptance rate by more than 30%.

Noise of non diaphragmatic origin or artifactual signals are strongly correlated at zero time delay and equal in polarity between all pairs of electrodes 12. Hence, this noise of non diaphragmatic origin or artifactual signals appear as a common mode signal for all electrode pairs and therefore, are substantially reduced by the double subtraction technique.

In the following description, it should be considered that the flow and volume of air breathed by the patient can be measured by any commercially available system.

Neuro-ventilatory efficiency:

The neuro-ventilatory efficiency is obtained by relating the diaphragm EMGdi signal intensity to changes in lung volume, or by relating the lung volume to changes in diaphragm EMGdi signal intensity. Since the relationship between the diaphragm EMGdi signal intensity and the lung volume is not linear, this non-linearity is minimized by expressing:

- the intensity of the diaphragm EMGdi signal for a given volume change from end-expiratory lung volume, for example the EMGdi signal intensity obtained during 400 ml inspiration starting from end-expiratory lung volume (in the present disclosure, intensity is intended to encompass the mean, peak, median and total RMS intensity of the diaphragm EMGdi signal); or

- the lung volume obtained at a given diaphragm EMGdi signal intensity.

A relatively small tidal lung volume is suitable because the relationship between diaphragm EMGdi signal intensity and lung volume is relatively linear at this low range. Secondly, the use of a fixed, given tidal volume or diaphragm EMGdi signal intensity will protect against the non-linear influences and allows for a reliable estimation of relative changes in neuro-ventilatory efficiency.

In this manner, a ventilatory efficiency index expressing:

- the EMGdi signal intensity for a given inspiratory lung volume starting from the end-expiratory lung volume; or

- the lung volume for a given diaphragm EMGdi signal intensity;

is calculated. If the EMGdi signal intensity for the above mentioned given inspiratory lung volume or the lung volume for the above mentioned given diaphragm EMGdi signal intensity is changing, the above indicated index will also change and this change can be expressed in percentage (%). For example, using the diaphragm EMGdi signal intensity for the above mentioned fixed, given inspiratory lung volume, an increased EMGdi signal intensity for the above mentioned given inspiratory lung volume will increase the index but will express a reduction in the neuro-ventilatory efficiency, and a decreased EMGdi signal intensity for that given inspiratory lung volume will reduce the index but will express an improvement of the neuro-ventilatory efficiency.

In the following description, an example using the EMGdi signal intensity for a fixed, given inspiratory lung volume will be given. However, it is within the scope of the present invention to use the lung volume for a fixed, given diaphragm EMGdi signal intensity.

Referring now to Figure 10 a preferred, practical embodiment is described. A neuro-ventilatory efficiency computation device 601 receives the signal 508 of Figure 5 as well as the given, fixed inspiratory lung volume. Device 601 comprises a unit 602 for determining

the intensity of the signal 508 for the given inspiratory lung volume. Although it is not illustrated, it is within the scope of the present invention to calculate, in unit 602, the peak, mean, median or any other intensity measure of signal 508 for the given inspiratory lung volume. If the intensity of signal 508 for the given inspiratory lung volume has increased at least by a given percentage (step 603), i.e. the neuro-ventilatory efficiency index has increased at least by said given percentage, the pressure, flow, or volume assist unit 604 is controlled by a unit 606 in view of increasing the magnitude of the pressure assist to the patient by a preset increment until the intensity of the signal 508 for the given inspiratory lung volume is restored to a predetermined, preset value.

Still referring to Figure 10, if the intensity for the given inspiratory lung volume has decreased at least by a given percentage (step 607), i.e. the neuro-ventilatory efficiency index has decreased at least by said given percentage, the pressure assist unit 604 is controlled by the unit 608 in view of decreasing the magnitude of the pressure assist by a preset increment until the intensity of the signal 508 for the given inspiratory lung volume is restored to the predetermined, preset value. Although it is not illustrated, it is within the scope of the present invention to calculate, in unit 602, the peak, mean, median or any other intensity measure of signal 508 for the given inspiratory lung volume, instead of the intensity of this signal. Also, the signals at the outputs of the units 606 and 608 can be used to generate an alarm or to manually adjust the pressure, flow or volume assist to the patient.

The response time is adjustable. The time base used to calculate trends in the EMG intensity for a given volume or vice versa

and used for the corrections is relatively slow (minutes) and the levels of applied support can be limited within a safe range. Again, an alarm can be generated or the pressure assist can be manually or automatically adjusted.

The pressure, flow, or volume assist unit 604 can be any device which can be controlled to generate any airway pressure of adjustable magnitude, for example any source of compressed gas, or a flow or volume pump. Of course, airway 605 refers to or, to the least, includes the patient's respiratory airway.

In this manner, the pressure assist unit 604 provides a pressure, flow, or volume assist that is adjusted in proportion to changed in neuro-ventilatory efficiency which is the EMGdi signal intensity at a given lung volume or vice versa. The pressure, flow, or volume assist unit continuoulsy operates to maintain a tracheal pressure, flow or volume that is adjusted in proportion to changes in neuro-ventilatory efficiency which is the EMGdi signal intensity at a given lung volume or vice versa.

Pre-inspiratory breathing effort:

A common problem with mechanically ventilated patients is that the patients' inspiratory effort will not immediately cause an inspiratory airflow so called "intrinsic PEEP" or "auto PEEP" which leads to a decrease in the neuro-ventilatory efficiency. The effect of "intrinsic PEEP" can be counteracted by the application of an "extrinsic PEEP" . However, there are no easy applicable techniques to determine when the applied level of "extrinsic PEEP" is adequate. The level of pre-inspiratory

effort obtained through the EMGdi signal intensity (common noise level subtracted) during for example a 100 milliseconds (ms) period immediately preceding the onset of inspiratory flow can be used to indicate the presence of "intrinsic PEEP", and the level of applied "extrinsic PEEP" can be adjusted such that the level of pre-inspiratory effort is suppressed i.e the EMGdi signal intensity (common noise level subtracted) during the above mentioned 100 ms period before onset of inspiratory flow is close to zero. A feedback loop can then be used to maintain the level of pre-inspiratory effort suppressed by adjusting as explained above the level of "extrinsic PEEP".

Just a word to mention that the above mentioned period of 100 ms can be replaced by a longer or shorter time period immediately preceding the onset of inspiratory flow or by the neuro-ventilatory delay 800 (Figure 12b), i.e. the time period between the onset of EMG 801 (Figure 12b) and the onset of inspiratory flow 802 (Figure 12a).

Figure 11 of the appended drawings illustrates a preferred, practical embodiment 700.

In the embodiment 700, an integrator 713 is responsive to the RMS EMG signal 508 to continuously calculate the EMG intensity for the above mentioned 100 ms period or neuro-ventilatory delay 800.

Embodiment 700 also comprises an inspiratory flow detector 702 responsive to the patient's inspiratory flow 703 measured, as indicated in the foregoing description, through any commercially

available system, to produce an output signal 705 representative of EMG activity.

The embodiment 700 of Figure 11 also comprises a neuro-ventilatory delay calculator 704 responsive to (a) the detection of a RMS EMG signal intensity higher than the common noise level (5%), and (b) the detection of the onset of inspiratory flow by the detector 702 to calculate the neuro-ventilatory delay 800 (Figure 12b).

A detector 714 is responsive to the EMG intensity calculated by the integrator 713 to detect the level of EMG intensity 803 (Figure 12b) at the onset of inspiratory flow 802 (Figure 12a) to trigger an alarm 716 when the level of the EMG intensity 803 at the onset of inspiratory flow 802 is higher than a given limit (detector 715). Upon triggering of the alarm 716, the level of applied "extrinsic PEEP" is either automatically or manually increased (device 708).

The detector 714 is responsive to the EMG intensity calculated by the integrator 713 to detect the level of EMG intensity 803 (Figure 12b) at the onset of inspiratory flow 802 (Figure 12a) to trigger an alarm 720 when the level of the EMG intensity 803 at the onset of inspiratory flow 802 is lower than a given limit (detector 719). Upon triggering of the alarm 720, the level of applied "extrinsic PEEP" is either automatically or manually decreased (device 711).

It should be mentioned that feedback from the neuro-ventilatory delay or pre-inspiratory EMG activity can also be used to adjust the sensitivity of the ventilators trigger functions.

Again, the time base used for these corrections is preferably relatively slow (minutes) and the levels of "extrinsic PEEP" can be limited within a safe range.

The pressure assist unit 604 can be any device which can be controlled to generate any airway flow and/or pressure of adjustable magnitude, for example any source of compressed gas, or a flow or volume pump.

In this manner, the delay from the beginning of the mechanically ventilated patients' inspiratory effort to the onset of the inspiratory assist will be minimized.

Although the present invention has been described hereinabove with reference to preferred embodiments thereof, these embodiments can be modified at will, within the scope of the appended claims, without departing from the spirit and nature of the subject invention.

CLAIMS

1) A method for substantially removing a common noise signal portion from electrical signals produced by an electrical signal source having a polarity reversal region with a centre, said electrical signals having inverse polarities on opposite sides of the centre, said method comprising:

a) sensing a first electrical signal of a first polarity through first electrodes located on one side of the centre;

b) sensing a second electrical signal of a second polarity through second electrodes located on the other side of said centre;

c) sensing a third electrical signal through third electrodes located between said first electrodes and said second electrodes;

d) combining the first and second electrical signals into a combination signal; and

e) combining the combination signal and the third electrical signal into an output signal.

2) A method for substantially removing a common noise signal portion as recited in claim 1, wherein:

- said first and second polarities are opposite polarities;

- combining the first and second electrical signals comprises subtracting one of the first and second electrical signals from the other of said first and second electrical signals to produce a combination signal substantially free from said common noise signal portion; and

- combining the combination signal with the third electrical signal comprises adding the combination signal and the third electrical

signal to produce said output signal still substantially free from said common noise signal portion and thereby substantially prevent output signal loss.

3) A method for substantially removing a common noise signal portion as recited in claim 1 or 2, further comprising differentially amplifying said first electrical signal, differentially amplifying said second electrical signal, and differentially amplifying said third electrical signal.

4) A method for substantially removing a common noise signal portion as recited in claim 1, 2 or 3, wherein sensing of said first, second and third electrical signals comprises forming with said first, second and third electrodes a series of electrodes having an axis extending through the centre of the polarity reversal region substantially in the direction of polarity reversal.

5) A method for substantially removing a common noise signal portion as recited in claim 1, 2, 3 or 4, further comprising applying said output signal substantially free from said common noise signal portion to a ventilatory assistance system.

6) A method for substantially removing a common noise signal portion as recited in claim 1, 2, 3, 4 or 5, wherein sensing of said first, second and third electrical signals comprises sensing first, second and third electromyographic signals, respectively, from at least one muscle of a patient, said at least one muscle constituting the electrical signal source.

7) A device for substantially removing a common noise signal portion from electrical signals produced by an electrical signal source having a polarity reversal region with a centre, said electrical signals having inverse polarities on opposite sides of the centre, said device comprising:

a) a first input responsive to a first electrical signal having a first polarity sensed through first electrodes located on one side of the centre;

b) a second input responsive to a second electrical signal having a second polarity sensed through second electrodes located on the other side of said centre;

c) a third input responsive to a third electrical signal sensed through third electrodes located between the first electrodes and the second electrodes;

d) means for combining the first and second electrical signals into a combination signal; and

e) means for combining the combination signal and the third electrical signal into an output signal.

8) A device for substantially removing a common noise signal portion as recited in claim 7, wherein:

- said first and second polarities are opposite polarities;

- the first and second electrical signals combining means comprises means for subtracting one of the first and second electrical signals from the other of said first and second electrical signals to produce a combination signal substantially free from said common noise signal portion; and

- the means for combining the combination signal with the third electrical signal comprises means for adding the combination

signal and the third electrical signal to produce said output signal still substantially free from said common noise signal portion and thereby substantially prevent output signal loss.

9) A device for substantially removing a common noise signal portion as recited in claim 7 or 8, further comprising a first differential amplifier for amplifying said first electrical signal, a second differential amplifier for amplifying said second electrical signal, and third differential amplifier for amplifying said third electrical signal.

10) A device for substantially removing a common noise signal portion as recited in claim 7 or 8, wherein said first, second and third electrodes form a series of electrodes having an axis extending through the center of the polarity reversal region substantially in the direction of polarity reversal.

11) A device for substantially removing a common noise signal portion as recited in claim 7, 8 or 9, further comprising a ventilatory assistance system to which is supplied said output signal substantially free from said common noise signal portion.

12) A device for substantially removing a common noise signal portion as recited in claim 7, 8, 9, 10 or 11, further comprising means for extracting from said first, second and third electrical signals, a first, second and third electromyographic signals from at least one muscle of a patient, said at least one muscle constituting said electrical signal source.

13) A neuro-ventilatory efficiency computation method for monitoring/controlling the level of ventilatory assist produced by a ventilatory assistance system, comprising:

a) receiving a first signal representative of inspiratory effort and having a first amplitude;

b) receiving a second signal representative of a lung volume and having a second amplitude;

c) calculating a relation between said first and second amplitudes at predetermined intervals; and

d) increasing or decreasing the ventilatory assist level depending on whether a present calculated value of said relation is higher or lower than a past calculated value of said relation by an amount exceeding a given threshold.

14) A neuro-ventilatory efficiency computation method as in claim 13, wherein said relation calculating comprises calculating a ratio between said first and second amplitudes at predetermined time intervals.

15) A neuro-ventilatory efficiency computation method as in claim 13, wherein said relation calculating comprises calculating a ratio between said first and second amplitudes at intervals when one of said first and second amplitudes reaches a predetermined level.

16) A neuro-ventilatory efficiency computation method as in claim 13, 14 or 15, wherein the ventilatory assist level increasing or decreasing comprises increasing the ventilatory assist level when said present calculated value of said relation is higher than said past calculated value of said relation by an amount exceeding the given threshold, and

decreasing the ventilatory assist level when said present calculated value of said relation is lower than said past calculated value of said relation by an amount exceeding said given threshold.

17) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15 or 16, wherein receiving the second signal representative of a lung volume comprises receiving a signal representative of a given lung volume.

18) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16 or 17, wherein receiving the first signal representative of inspiratory effort comprises receiving a signal representative of a given level of inspiratory effort.

19) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17 or 18, further comprising generating an alarm signal when said present calculated value of said relation is higher or lower than the past calculated value of said relation by an amount exceeding said given threshold.

20) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17, 18, or 19, comprising manually performing said increasing or decreasing of the ventilatory assist level.

21) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17, 18, 19 or 20, comprising expressing the first signal representative of inspiratory effort as one of the following values: a mean

of said first amplitude, a median of said first amplitude, and a peak of said first amplitude.

22) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17, 18, 19 or 20, comprising expressing the second signal representative of a lung volume as one of the following values: a mean of said second amplitude, a median of said second amplitude, and a peak of said second amplitude.

23) A neuro-ventilatory efficiency computation method as in claim 13, 14, 15, 16, 17, 18, 19, 20, 21 or 22 wherein receiving the first signal representative of inspiratory effort comprises receiving an electromyographic signal from at least one muscle of a patient.

24) A neuro-ventilatory efficiency computation device for monitoring/controlling the level of ventilatory assist produced by a ventilatory assistance system, comprising:

a) a first input for receiving a first signal representative of inspiratory effort and having a first amplitude;

b) a second input for receiving a second signal representative of a lung volume and having a second amplitude;

c) means for calculating a relation between said first and second amplitudes at predetermined intervals; and

d) means for increasing or decreasing the ventilatory assist level depending on whether a present calculated value of said relation is higher or lower than a past calculated value of said relation by an amount exceeding a given threshold.

25) A neuro-ventilatory efficiency computation device as in claim 24, wherein:

the calculating means comprises a divider responsive to the first and second amplitudes for calculating a ratio between said first and second amplitudes at predetermined intervals;

the increasing or decreasing means comprises:

- a comparator responsive to the present calculated value and the past calculated value of said relation for producing a signal representative of a comparison between a present calculated value of said relation and a past calculated value of said relation;
- an adder interposed between the comparator and the ventilatory assistance system for adding a preset increment to or subtracting a preset decrement from said ventilatory assist level when the comparison signal exceeds a given threshold.

26) A neuro-ventilatory efficiency computation device as in claim 24 or 25, wherein said calculating means comprises means for calculating said relation at predetermined time intervals.

27) A neuro-ventilatory efficiency computation device as in claim 24, or 25, wherein said calculating means comprises means for calculating said relation at intervals when one of said first and second amplitudes reach a predetermined level.

28) A neuro-ventilatory efficiency computation device as in any one of claims 25 to 27, wherein said adder comprises means for adding said preset increment to said ventilatory assist level when said present calculated value of said relation is higher than said past calculated value

of said relation by an amount exceeding said given threshold, and means for subtracting said preset decrement from said ventilatory assist level when said present calculated value of said relation is lower than said past calculated value of said relation by an amount exceeding said given threshold.

29) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 28, wherein the second signal representative of a lung volume is a signal representative of a given lung volume.

30) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 28, wherein the second signal representative of inspiratory effort is a signal representative of a given level of inspiratory effort.

31) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 30, further comprising an alarm generator to produce an alarm signal when said present calculated value of said relation is higher or lower than the past calculated value of said relation by an amount exceeding said given threshold.

32) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 31, wherein said adder comprises a manual adjustment system to add said preset increment to or subtracting said preset decrement from said ventilatory assist level.

33) A neuro-ventilatory efficiency computation device as in any one of claims 22 to 32, comprising means for expressing the first signal representative of inspiratory effort by means of one of the following

values: a mean of said first amplitude, a median of said first amplitude, and a peak of said first amplitude.

34) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 32, further comprising means for expressing the second signal representative of a lung volume by means of one of the following values: a mean of said second amplitude, a median of said second amplitude, and a peak of said second amplitude.

35) A neuro-ventilatory efficiency computation device as in any one of claims 24 to 34, wherein the first signal representative of inspiratory effort is an electromyographic signal from at least one muscle of a patient.

36) A method for monitoring/adjusting the level of positive end expiratory pressure produced by a pressure assist device in relation to a signal representative of inspiratory effort in view of minimizing the level of pre-inspiratory effort, comprising:

a) receiving a signal representative of inspiratory flow;

b) calculating from said inspiratory flow signal an onset time for inspiration;

c) receiving a signal representative of inspiratory effort having an amplitude;

d) calculating a signal representative of pre-inspiratory effort in response to said onset time and said signal representative of inspiratory effort; and

e) increasing or decreasing the level of positive end expiratory pressure in relation to said signal representative of pre-inspiratory effort .

37) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 36, wherein increasing or decreasing the level of positive end expiratory pressure comprises increasing or decreasing the level of positive end expiratory pressure depending on whether the amplitude of said signal representative of pre-inspiratory effort is higher or lower than a given threshold.

38) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 37, wherein increasing of decreasing the level of positive end expiratory pressure comprises increasing the level of positive end expiratory pressure when said signal representative of pre-inspiratory effort is higher than said given threshold, and decreasing the level of positive end expiratory pressure when said signal representative of pre-inspiratory effort is lower than said given threshold.

39) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 38, wherein increasing or decreasing the level of positive end expiratory pressure comprises increasing or decreasing one of the following parameters produced by said pressure assist device: a level of air flow, and a level of air volume.

40) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 39, wherein calculating said signal representative of pre-inspiratory effort comprises

calculating said signal representative of pre-inspiratory effort at said onset time.

41) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 39, wherein calculating said signal representative of pre-inspiratory effort comprises calculating said signal representative of pre-inspiratory effort during a period between the time when said signal representative of inspiratory effort reaches a minimum amplitude and said onset time.

42) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 39, wherein:

a) calculating said signal representative of pre-inspiratory effort comprises calculating a period between the time when said signal representative of inspiratory effort reaches a minimum amplitude and said onset time; and

b) increasing or decreasing the level of positive end expiratory pressure comprises increasing or decreasing the level of positive end expiratory pressure depending on whether said period is higher or lower than a given limit.

43) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 39, wherein increasing or decresing the level of positive end expiratory pressure comprises increasing or decreasing the level of positive end expiratory pressure depending on both whether said period is higher or lower than the given limit, and whether the amplitude of the signal representative of pre-inspiratory effort is higher or lower than a given threshold.

44) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 43, further comprising generating an alarm signal when said signal representative of pre-inspiratory effort is higher or lower than a given threshold.

45) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 44, comprising manually performing the increase or decrease of the level of positive end expiratory pressure.

46) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 45, comprising expressing said signal representative of inspiratory effort as one of the following values: a mean amplitude, a median amplitude, and a peak amplitude.

47) A method for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 36 to 46, wherein receiving said signal representative of inspiratory effort comprises receiving an electromyographic signal from at least one muscle of a patient.

48) A controller for monitoring/adjusting the level of positive end expiratory pressure produced by a pressure assist device in relation to a signal representative of inspiratory effort in view of minimizing the level of pre-inspiratory effort, comprising:

a) a first input for receiving a signal representative of inspiratory flow having an onset time for inspiration;

b) a second input for receiving a signal representative of inspiratory effort having an amplitude;

c) a computer device responsive to said onset time and said signal representative of inspiratory effort to compute said signal representative of pre-inspiratory effort; and

d) an adder/substractor for adding a preset increment to or subtracting a preset decrement from the level of positive end expiratory pressure in relation to said signal representative of pre-inspiratory effort .

49) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 48, wherein the adder/subtractor comprises means for adding the preset increment to or for subtracting the preset decrement from the level of positive end expiratory pressure depending on whether the amplitude of said signal representative of pre-inspiratory effort is higher or lower than a given threshold.

50) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 49, wherein the adder/subtractor comprises means for adding the preset increment to the level of positive end expiratory pressure when the signal representative of pre-inspiratory effort is higher than said given threshold, and means for subtracting the preset decrement from the level of positive end expiratory pressure when said signal representative of pre-inspiratory effort is lower than said given threshold.

51) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 50, wherein adder/subtractor comprises means for adding the preset increment to or subtracting the preset decrement from one of the following parameters produced by said pressure assist device: a level of air flow, and a level of air volume.

52) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 51, wherein said computer device comprises means for calculating said signal representative of pre-inspiratory effort at said onset time.

53) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 51, wherein said computer device comprises means for calculating said signal representative of pre-inspiratory effort during a period between the time when said signal representative of inspiratory effort reaches a minimum amplitude and said onset time.

54) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 51, wherein:

a) said computer device comprises means for calculating a period between the time when said signal representative of inspiratory effort reaches a minimum amplitude and said onset time; and

b) said adder/subtractor comprises means for adding said preset increment to or for subtracting said preset decrement from the level of positive end expiratory pressure depending on whether said period is higher or lower than a given limit.

55) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in claim 54, wherein said adding/subtracting means comprise means for adding the preset increment to or for subtracting the preset decrement from the level of positive end expiratory pressure depending on both whether said period is higher or lower than a given limit, and whether the amplitude of said signal representative of pre-inspiratory effort is higher or lower than a given threshold.

56) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 55, further comprising an alarm generator to produce an alarm signal when said signal representative of pre-inspiratory effort is higher or lower than a given threshold.

57) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 56, wherein said adder comprises a manual adjustment system for adding said preset increment to or subtracting said preset decrement from the level of positive end expiratory pressure.

58) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 57, comprising means for expressing the signal representative of inspiratory effort as one of the following values: a mean amplitude, a median amplitude, and a peak amplitude.

59) A controller for monitoring/adjusting the level of positive end expiratory pressure as defined in any one of claims 48 to 58, wherein the signal representative of inspiratory effort is an electromyographic signal from at least one muscle of a patient.

ABSTRACT OF THE DISCLOSURE

A closed loop system uses (a) the intensity of the diaphragm electromyogram (EMG) for a given inspiratory volume; (b) the inspiratory volume for a given EMG intensity; or (c) a combination of (a) and (b); in view of controlling the level of gas flow, gas volume or gas pressure delivered by a mechanical (lung) ventilator. The closed loop ventilator system enables for automatic or manual adjustment of the level of inspiratory support in proportion to changes in the neuro-ventilatory efficiency such that the neural drive remains stable at a desired target level. An alarm can also be used to detect changes in neuroventilatory efficiency in view of performing manual adjustments.

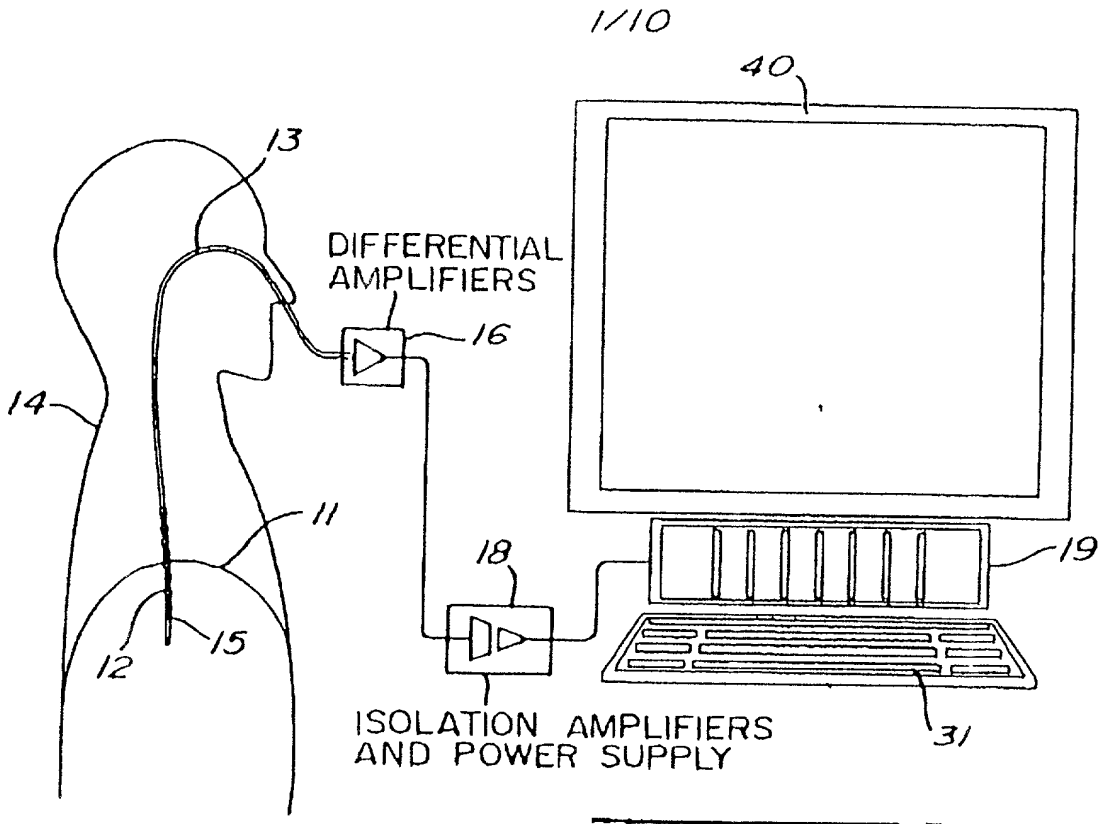

Fig. 1

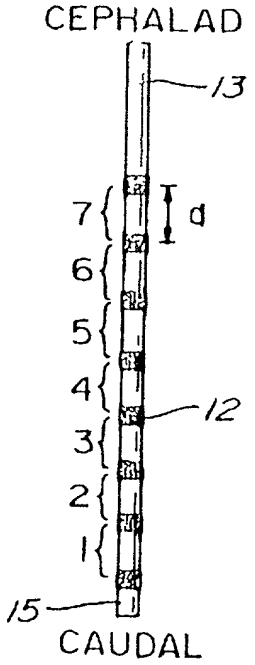

Fig. 2

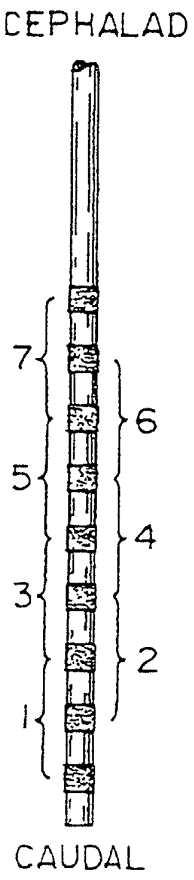

FIG. 3

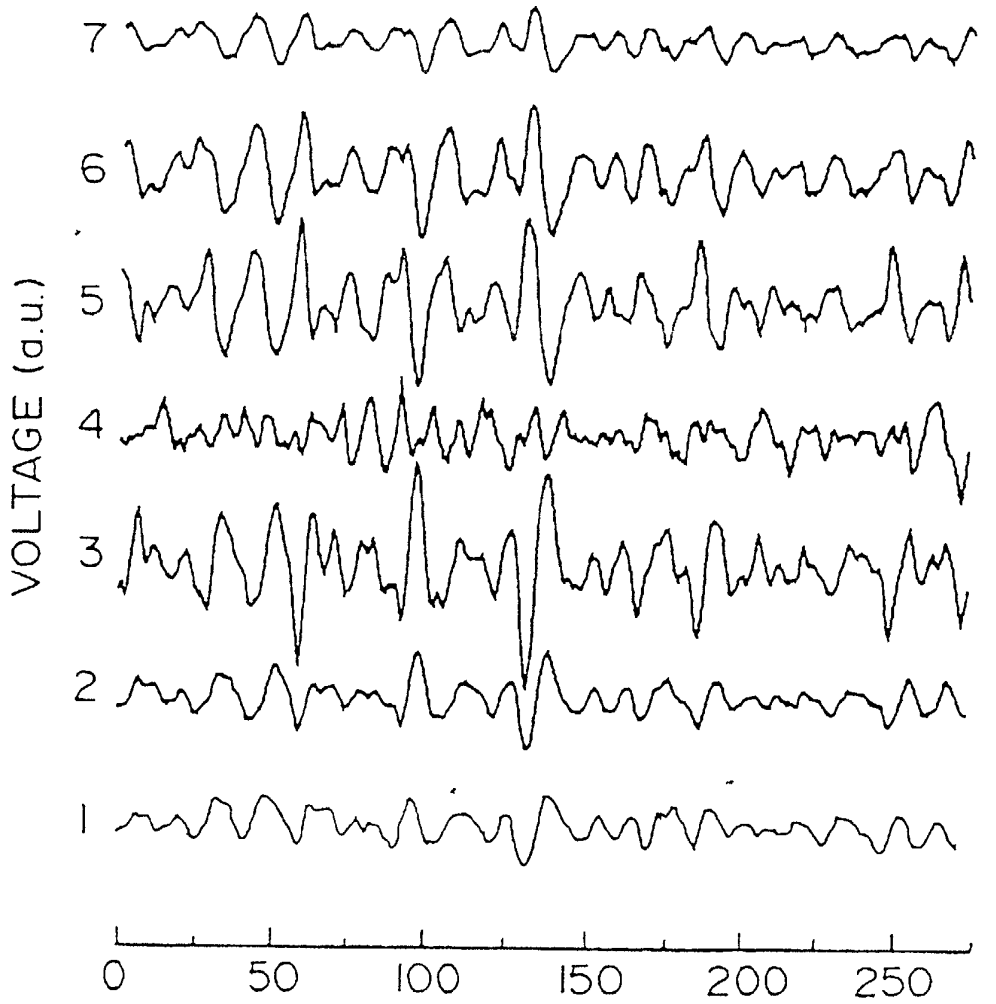

FIG. 4

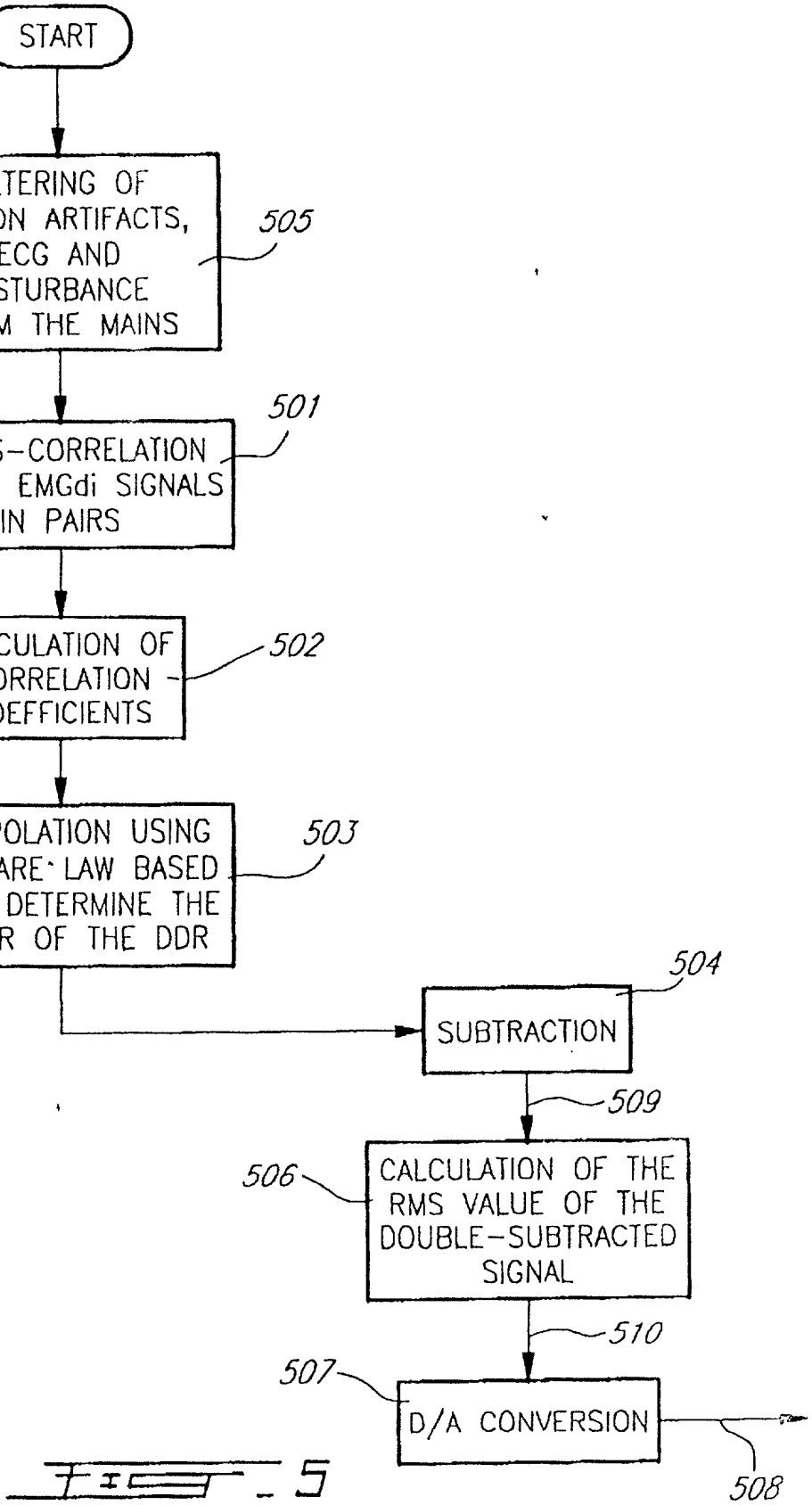
START
FILTERING OF MOTION ARTIFACTS, ECG AND DISTURBANCE FROM THE MAINS
505
CROSS-CORRELATION OF THE EMGdi SIGNALS IN PAIRS
501
CALCULATION OF CORRELATION COEFFICIENTS
502
INTERPOLATION USING A SQUARE-LAW BASED FIT TO DETERMINE THE CENTER OF THE DDR
503
SUBTRACTION
504
509
CALCULATION OF THE RMS VALUE OF THE DOUBLE-SUBTRACTED SIGNAL
506
510
D/A CONVERSION
507
508

Fig. 5

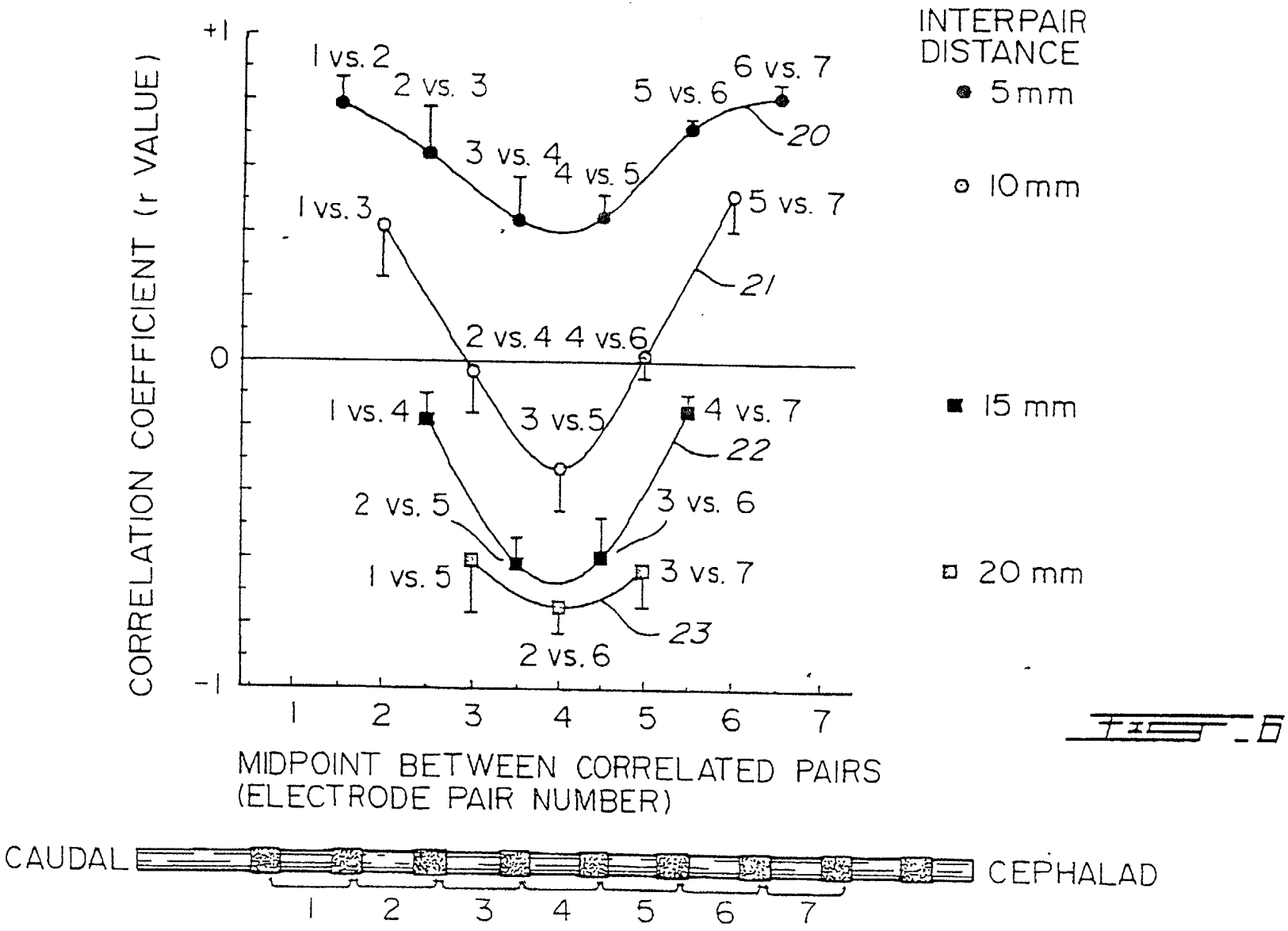

Fig. 6

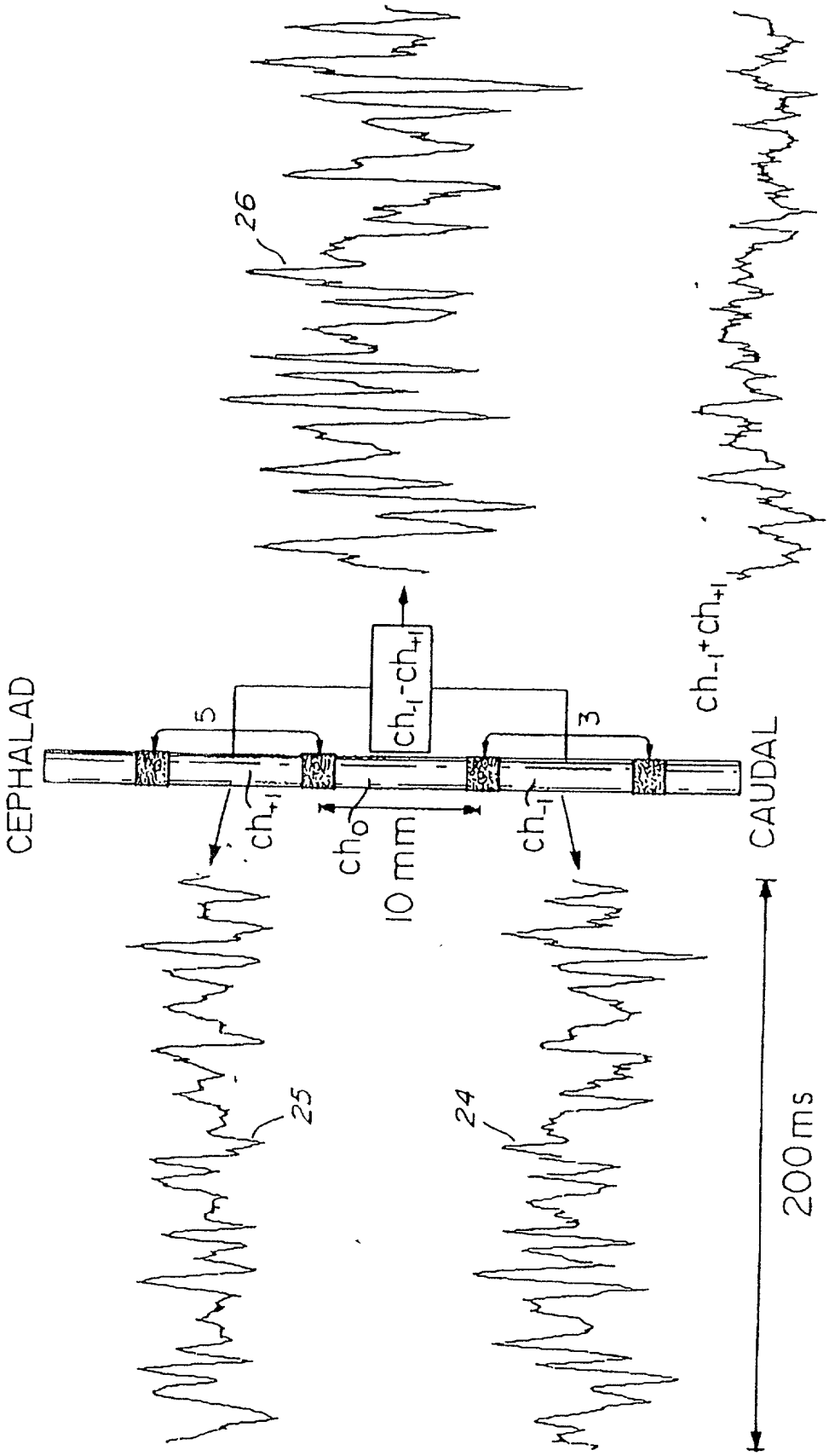

FIG -7

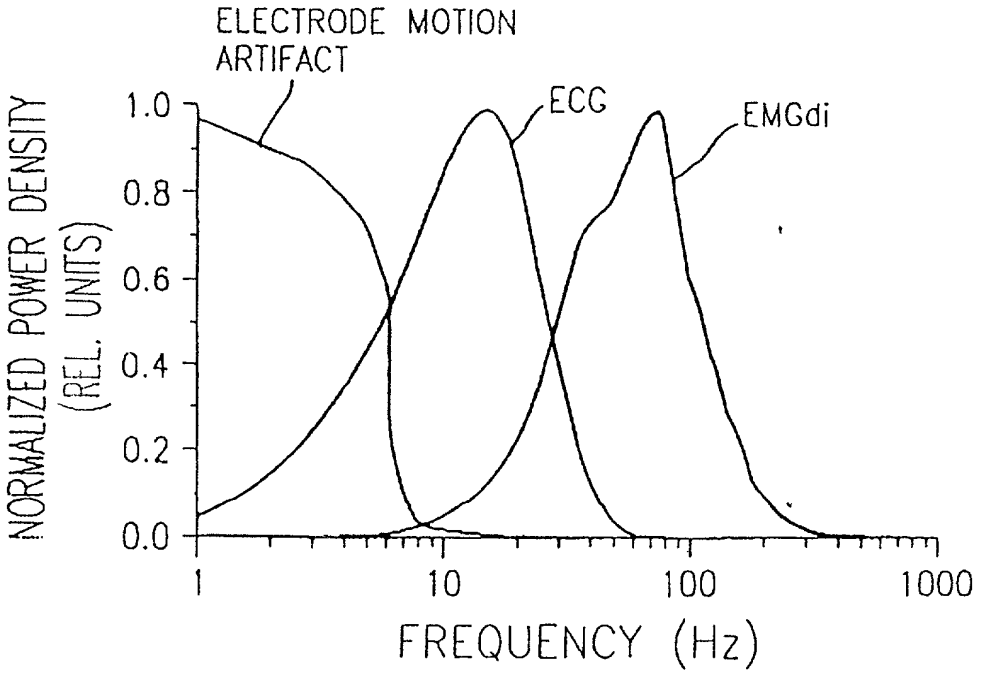

Fig. 8a

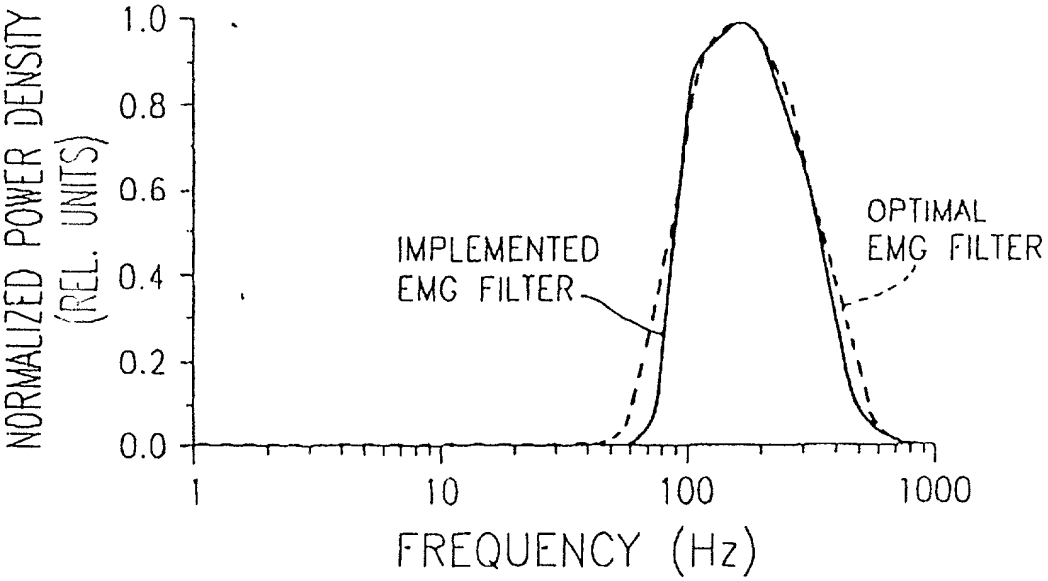

Fig. 8b

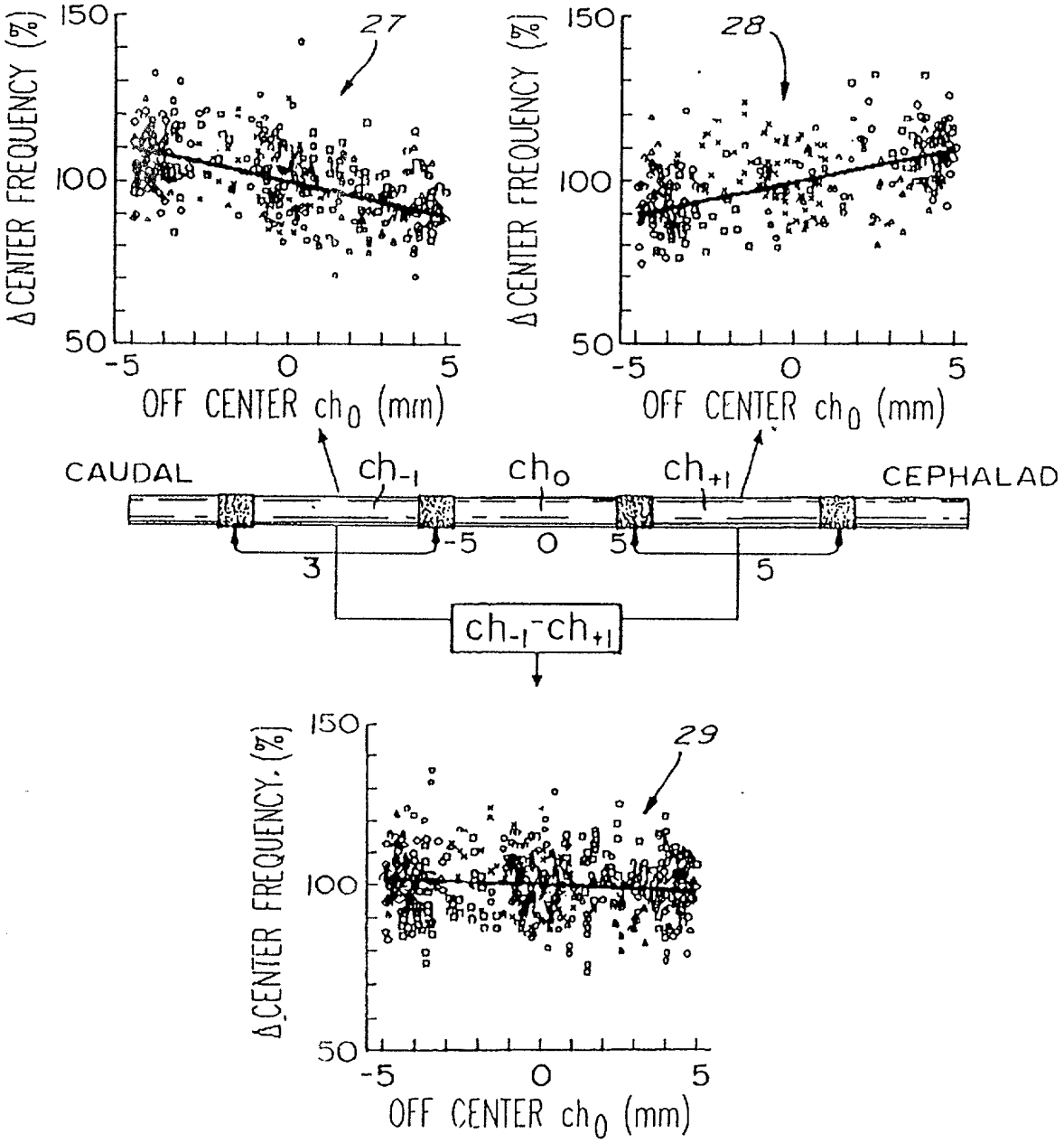

FIG. 9

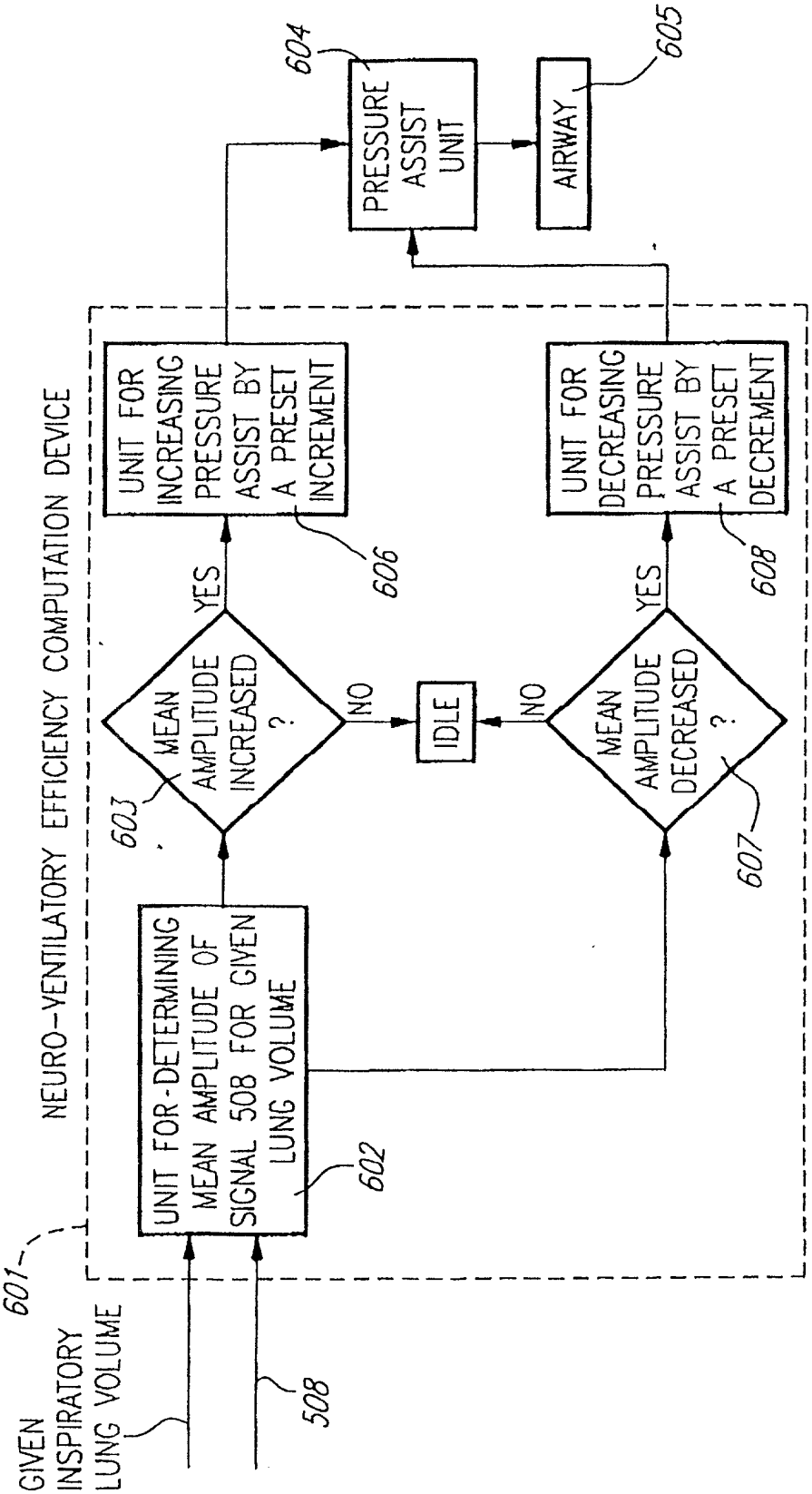
GIVEN INSPIRATORY LUNG VOLUME
508
601
NEURO-VENTILATORY EFFICIENCY COMPUTATION DEVICE
UNIT FOR-DETERMINING MEAN AMPLITUDE OF SIGNAL 508 FOR GIVEN LUNG VOLUME
602
MEAN AMPLITUDE INCREASED ?
603
YES
NO
UNIT FOR INCREASING PRESSURE ASSIST BY A PRESET INCREMENT
606
IDLE
MEAN AMPLITUDE DECREASED ?
607
YES
NO
UNIT FOR DECREASING PRESSURE ASSIST BY A PRESET DECREMENT
608
PRESSURE ASSIST UNIT
604
AIRWAY
605

Fig. 10

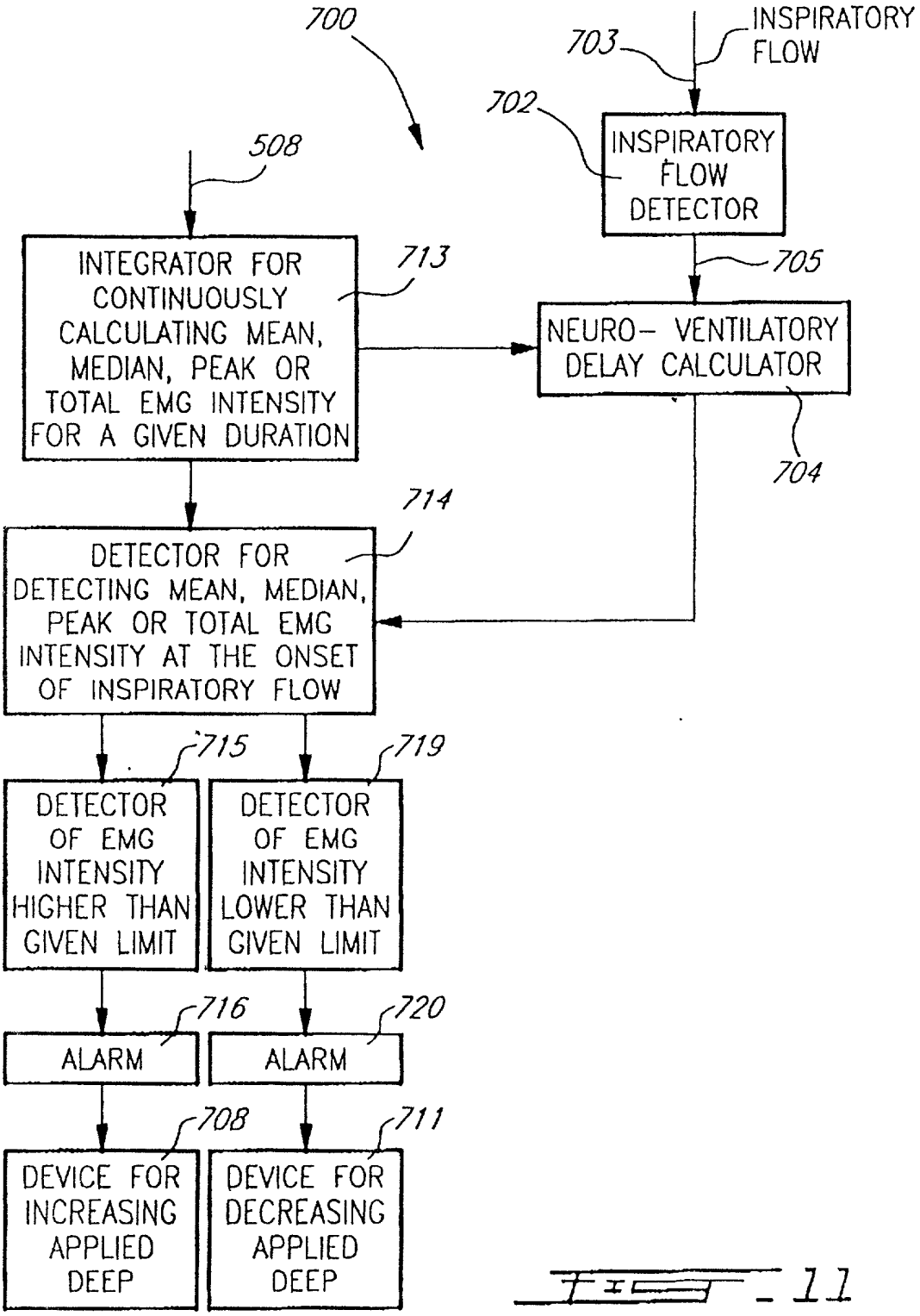
700
703
INSPIRATORY FLOW
702
INSPIRATORY FLOW DETECTOR
508
705
INTEGRATOR FOR CONTINUOUSLY CALCULATING MEAN, MEDIAN, PEAK OR TOTAL EMG INTENSITY FOR A GIVEN DURATION
713
NEURO- VENTILATORY DELAY CALCULATOR
704
714
DETECTOR FOR DETECTING MEAN, MEDIAN, PEAK OR TOTAL EMG INTENSITY AT THE ONSET OF INSPIRATORY FLOW
715
719
DETECTOR OF EMG INTENSITY HIGHER THAN GIVEN LIMIT
DETECTOR OF EMG INTENSITY LOWER THAN GIVEN LIMIT
716
720
ALARM
ALARM
708
711
DEVICE FOR INCREASING APPLIED DEEP
DEVICE FOR DECREASING APPLIED DEEP

Fig. 11

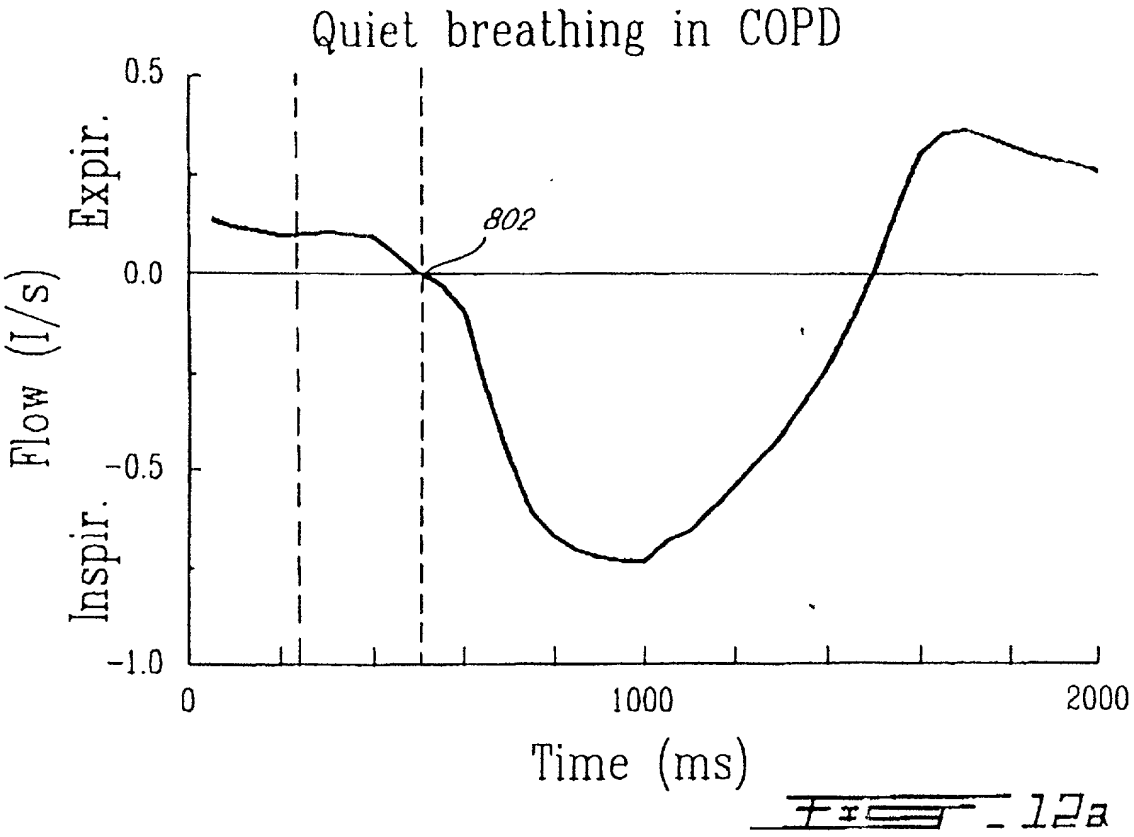

Fig 12a

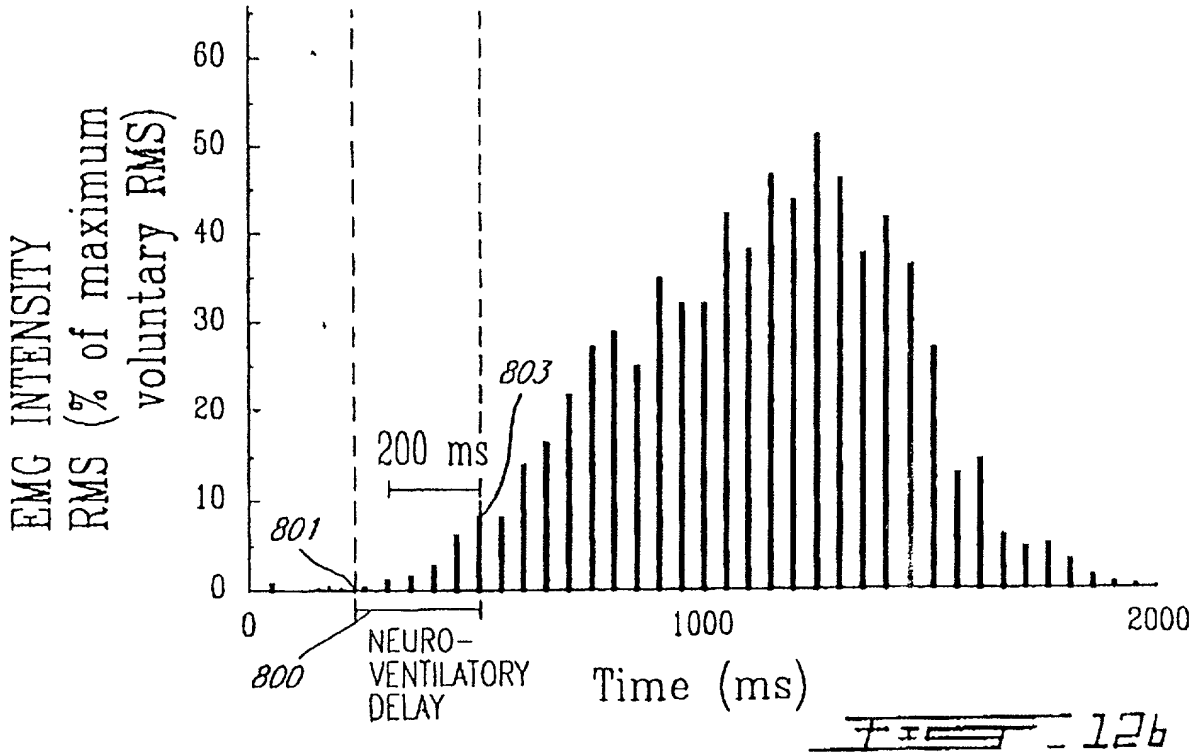

Fig 12b

Practitioner's Docket No. 776-009999-US(PAR) **PATENT**

COMBINED DECLARATION AND POWER OF ATTORNEY

(ORIGINAL, DESIGN, NATIONAL STAGE OF PCT, SUPPLEMENTAL, DIVISIONAL, CONTINUATION, OR C-I-P)

As a below named inventor, I hereby declare that:

TYPE OF DECLARATION

This declaration is of the following type:

(check one applicable item below)

- ☐ original.
- ☐ design.
- ☐ supplemental.

NOTE: If the declaration is for an International Application being filed as a divisional, continuation or continuation-in-part application, do not check next item; check appropriate one of last three items.

- ☒ national stage of PCT.

NOTE: If one of the following 3 items apply, then complete and also attach ADDED PAGES FOR DIVISIONAL, CONTINUATION OR C-I-P.

NOTE: See 37 C.F.R. § 1.63(d) (continued prosecution application) for use of a prior nonprovisional application declaration in the continuation or divisional application being filed on behalf of the same or fewer of the inventors named in the prior application.

- ☐ divisional.
- ☐ continuation.

NOTE: Where an application discloses and claims subject matter not disclosed in the prior application, or a continuation or divisional application names an inventor not named in the prior application, a continuation-in-part application must be filed under 37 C.F.R. § 1.53(b) (application filing requirements — nonprovisional application).

- ☐ continuation-in-part (C-I-P).

INVENTORSHIP IDENTIFICATION

WARNING: *If the inventors are each not the inventors of all the claims, an explanation of the facts, including the ownership of all the claims at the time the last claimed invention was made, should be submitted.*

My residence, post office address and citizenship are as stated below, next to my name. I believe that I am the original, first and sole inventor *(if only one name is listed below)* or an original, first and joint inventor *(if plural names are listed below)* of the subject matter that is claimed, and for which a patent is sought on the invention entitled:

TITLE OF INVENTION

PROPORTIONAL PRESSURE ASSIST VENTILATION CONTROLLED BY A DIAPHRAGM ELECTROMYOGRAPHIC SIGNAL

SPECIFICATION IDENTIFICATION

the specification of which:

(complete (a), (b), or (c))

(a) ☐ is attached hereto.

NOTE: *"The following combinations of information supplied in an oath or declaration filed on the application filing date with a specification are acceptable as minimums for identifying a specification and compliance with any one of the items below will be accepted as complying with the identification requirement of 37 CFR 1.63:*

"(1) name of inventor(s), and reference to an attached specification which is both attached to the oath or declaration at the time of execution and submitted with the oath or declaration on filing;

"(2) name of inventor(s), and attorney docket number which was on the specification as filed; or

"(3) name of inventor(s), and title which was on the specification as filed."

Notice of July 13, 1995 (1177 O.G. 60).

(b) ☐ was filed on _____, as ☒ Serial No. 09 / 701,824
or ☐ _____
and was amended on _____ *(if applicable).*

NOTE: *Amendments filed after the original papers are deposited with the PTO that contain new matter are not accorded a filing date by being referred to in the declaration. Accordingly, the amendments involved are those filed with the application papers or, in the case of a supplemental declaration, are those amendments claiming matter not encompassed in the original statement of invention or claims. See 37 CFR 1.67.*

NOTE: *"The following combinations of information supplied in an oath or declaration filed after the filing date are acceptable as minimums for identifying a specification and compliance with any one of the items below will be accepted as complying with the identification requirement of 37 CFR 1.63:*

"(1) name of inventor(s), and application number (consisting of the series code and the serial number; e.g., 08/123,456);

"(2) name of inventor(s), serial number and filing date;

"(3) name of inventor(s) and attorney docket number which was on the specification as filed;

"(4) name of inventor(s), title which was on the specification as filed and filing date;

"(5) name of inventor(s), title which was on the specification as filed and reference to an attached specification which is both attached to the oath or declaration at the time of execution and submitted with the oath or declaration; or

"(6) name of inventor(s), title which was on the specification as filed and accompanied by a cover letter accurately identifying the application for which it was intended by either the application number (consisting of the series code and the serial number; e.g., 08/123,456), or serial number and filing date. Absent any statement(s) to the contrary, it will be presumed that the application filed in the PTO is the application which the inventor(s) executed by signing the oath or declaration."

Notice of July 13, 1995 (1177 O.G. 60).

(c) ☒ was described and claimed in PCT International Application No. PCT/CA99/00529 filed on June 4, 1999 and as amended under PCT Article 19 on _____ *(if any).*

SUPPLEMENTAL DECLARATION (37 C.F.R. § 1.67(b))

(complete the following where a supplemental declaration is being submitted)

☐ I hereby declare that the subject matter of the

- ☐ attached amendment
- ☐ amendment filed on ______________

was part of my/our invention and was invented before the filing date of the original application, above-identified, for such invention.

ACKNOWLEDGEMENT OF REVIEW OF PAPERS AND DUTY OF CANDOR

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information, which is material to patentability as defined in 37, Code of Federal Regulations, § 1.56,

(also check the following items, if desired)

☒ and which is material to the examination of this application, namely, information where there is a substantial likelihood that a reasonable Examiner would consider it important in deciding whether to allow the application to issue as a patent, and

- ☐ In compliance with this duty, there is attached an information disclosure statement, in accordance with 37 CFR 1.98.

PRIORITY CLAIM (35 U.S.C. §§ 119(a)-(d))

NOTE: *"The claim to priority need be in no special form and may be made by the attorney or agent if the foreign application is referred to in the oath or declaration as required by § 1.63. The claim for priority and the certified copy of the foreign application specified in 35 U.S.C. 119(b) must be filed in the case of an interference (§ 1.630), when necessary to overcome the date of a reference relied upon by the examiner, when specifically required by the examiner, and in all other situations, before the patent is granted. If the claim for priority or the certified copy of the foreign application is filed after the date the issue fee is paid, it must be accompanied by a petition requesting entry and by the fee set forth in § 1.17(i). If the certified copy is not in the English language, a translation need not be filed except in the case of interference; or when necessary to overcome the date of a reference relied upon by the examiner; or when specifically required by the examiner, in which event an English language translation must be filed together with a statement that the translation of the certified copy is accurate." 37 C.F.R. § 1.55(a).*

I hereby claim foreign priority benefits under Title 35, United States Code, §§ 119(a)-(d) of any foreign application(s) for patent or inventor's certificate or of any PCT International application(s) designating at least one country other than the United States of America listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT International application(s) designating at least one country other than the United States of America filed by me on the same subject matter having a filing date before that of the application(s) of which priority is claimed.

(complete (d) or (e))

(d) ☐ no such applications have been filed.

(e) ☒ such applications have been filed as follows.

NOTE: *Where item (c) is entered above and the International Application which designated the U.S. itself claimed priority check item (e), enter the details below and make the priority claim.*

PRIOR FOREIGN/PCT APPLICATION(S) FILED WITHIN 12 MONTHS (6 MONTHS FOR DESIGN) PRIOR TO THIS APPLICATION AND ANY PRIORITY CLAIMS UNDER 35 U.S.C. § 119(a)-(d)

COUNTRY (OR INDICATE IF PCT)	APPLICATION NUMBER	DATE OF FILING (day, month, year)	PRIORITY CLAIMED UNDER 37 USC 119
			☐ YES NO ☐
			☐ YES NO ☐
			☐ YES NO ☐
			☐ YES NO ☐
			☐ YES NO ☐

CLAIM FOR BENEFIT OF PRIOR U.S. PROVISIONAL APPLICATION(S)

(34 U.S.C. § 119(e))

I hereby claim the benefit under Title 35, United States Code, § 119(e) of any United States provisional application(s) listed below:

PROVISIONAL APPLICATION NUMBER	FILING DATE
_____ /_____	_____
_____ /_____	_____
_____ /_____	_____

CLAIM FOR BENEFIT OF EARLIER US/PCT APPLICATION(S) UNDER 35 U.S.C. 120

☐ The claim for the benefit of any such applications are set forth in the attached ADDED PAGES TO COMBINED DECLARATION AND POWER OF ATTORNEY FOR DIVISIONAL, CONTINUATION OR CONTINUATION-IN PART (C-I-P) APPLICATION.

ALL FOREIGN A. PLICATION(S), *IF ANY*, FILED MOR. THAN 12 MONTHS (6 MONTHS FOR DESIGN) PRIOR TO THIS U.S. APPLICATION

PCT/CA99/00529 filed 4 June 1999

Canada - 2,239,673 filed 4 June 1998

NOTE: *If the application filed more than 12 months from the filing date of this application is a PCT filing forming the basis for this application entering the United States as (1) the national stage, or (2) a continuation, divisional, or continuation-in-part, then also complete ADDED PAGES TO COMBINED DECLARATION AND POWER OF ATTORNEY FOR DIVISIONAL, CONTINUATION OR C-I-P APPLICATION for benefit of the prior U.S. or PCT application(s) under 35 U.S.C. § 120.*

POWER OF ATTORNEY

I hereby appoint the following practitioner(s) to prosecute this application and transact all business in the Patent and Trademark Office connected therewith.

(list name and registration number)

(3)

Clarence A. Green (24,622)
Mark F. Harrington (31,686)
Janik Marcovici (42,841)

(check the following item, if applicable)

☐ I hereby appoint the practitioner(s) associated with the Customer Number provided below to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith.

☐ Attached, as part of this declaration and power of attorney, is the authorization of the above-named practitioner(s) to accept and follow instructions from my representative(s).

SEND CORRESPONDENCE TO

☒ Address

Clarence A. Green
PERMAN & GREEN, LLP
425 Post Road
Fairfield, CT 06430

☐ Customer Number 2512

DIRECT TELEPHONE CALLS TO:
(Name and telephone number)

Clarence A. Green
(203) 259-1800

DECLARATION

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

SIGNATURE(S)

NOTE: Carefully indicate the family (or last) name, as it should appear on the filing receipt and all other documents.

1-00

Full name of sole or first inventor

Christer (GIVEN NAME) _____ (MIDDLE INITIAL OR NAME) SINDERBY (FAMILY (OR LAST NAME))

Inventor's signature _____

Date 20 april 2001 Country of Citizenship ~~Canada~~ Sweden

Residence 12750, 27th Avenue, Montreal, Quebec H1E 1Z9, Canada CAX

Post Office Address 12750, 27th Avenue, Montreal, Quebec H1E 1Z9, Canada

2-00

Full name of second joint inventor, if any

Jennifer (GIVEN NAME) _____ (MIDDLE INITIAL OR NAME) BECK (FAMILY (OR LAST NAME))

Inventor's signature _____

Date 20 april 2001 Country of Citizenship Canada

Residence 12750, 27th Avenue, Montreal, Quebec H1E 1Z9, Canada CAX

Post Office Address 12750, 27th Avenue, Montreal, Quebec H1E 1Z9, Canada

Full name of third joint inventor, if any

(GIVEN NAME) _____ (MIDDLE INITIAL OR NAME) _____ (FAMILY (OR LAST NAME)) _____

Inventor's signature _____

Date _____ Country of Citizenship _____

Residence _____

Post Office Address _____

(ch proper box(es) for any of the following xd page(s) that form a part of this declaration)

☐ **Signature** for fourth and subsequent joint inventors. *Number of pages added* _____

• • •

☐ **Signature** by administrator(trix), executor(trix) or legal representative for deceased or incapacitated inventor. *Number of pages added* _____.

• • •

☐ **Signature** for inventor who refuses to sign or cannot be reached by person authorized under 37 CFR 1.47. *Number of pages added* _____

• • •

☐ Added page for **signature** by one joint inventor on behalf of deceased inventor(s) where legal representative cannot be appointed in time. (37 CFR 1.47)

• • •

☐ Added pages to combined declaration and power of attorney for divisional, continuation, or continuation-in-part (C-I-P) application.

☐ Number of pages added _____

• • •

☐ Authorization of practitioner(s) to accept and follow instructions from representative.

• • •

(if no further pages form a part of this Declaration, then end this Declaration with this page and check the following item)

■ This declaration ends with this page.